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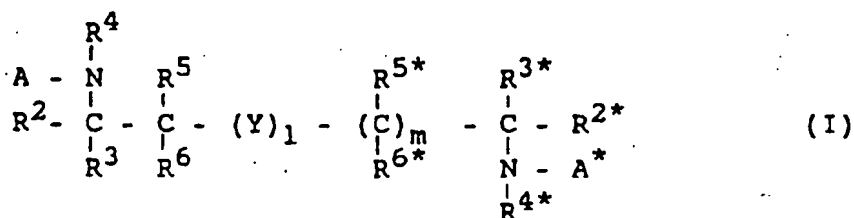
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## Inhibitors of retroviral proteases

The present invention concerns compounds of formula I



wherein

A, Y, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, l, m and the corresponding radicals indicated by \* are defined as stated in the description, a process for their preparation and their use for the inhibition of retroviral proteases.

## INHIBITORS OF RETROVIRAL PROTEASES

The present invention concerns substances which inhibit the action of retroviral proteases, processes for their preparation, their use and drugs containing them.

The etiological cause of acquired immune deficiency syndrome (AIDS) is the so-called human immunodeficiency virus (HIV) (F. Barre-Sinoussi, et al., Science 220, (1983), 868-870; R. C. Gallo, et al., Science 224, (1984), 500-

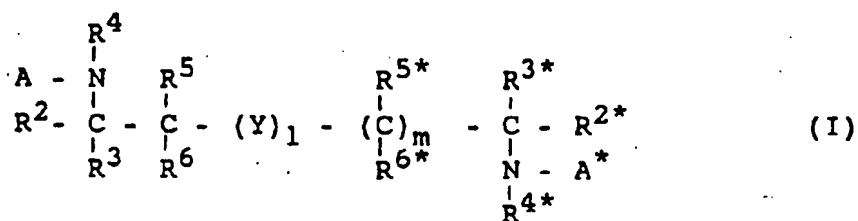


The HIV protease consists of 99 amino acids and obviously splits out by itself from the pol polyprotein through hydrolysis of the two phe-pro bonds in positions 68-69 and 167-168 (M. C. Graves, J. J. Lim, E. P. Heimer and R. A. Kramer, Proc. Natl. Acad. Sci. USA 85 (1988), 2449-2453; J. Hansen, S. Billich, T. Schulze, S. Sukrow and K. Mölling, EMBO J. 7 (1988), 1785-1791; E. P. Lillehoj, et al., J. Virology 62 (1988) 3053-3058; J. Schneider and S. B. H. Kent, Cell 54 (1988) 363-368).

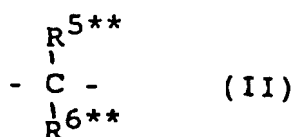
High doses of pepstatin A were able in biosynthesis to reduce the formation of the nucleoprotein p24 (v.d.Helm, L. Gürtler, J. Eberle an F. Deinhardt, FEBS Lett., 247, (1989), 349-352).

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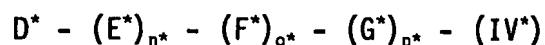
The present invention concerns compounds of formula I



wherein Y stands for oxygen, sulfur a radical of formula II or a radical of formula III



l and m, independent of each other, are 0 or 1; A means a radical of formula IV and A\* a radical of formula IV\*

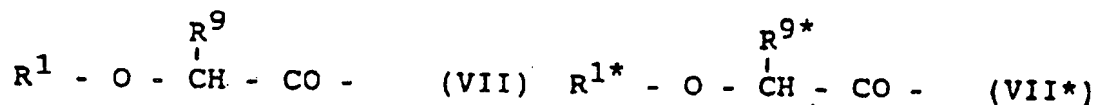
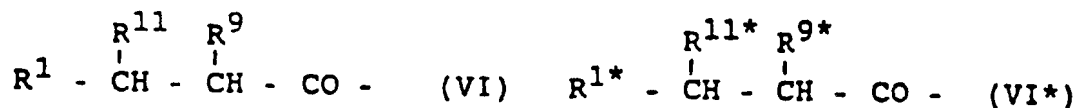
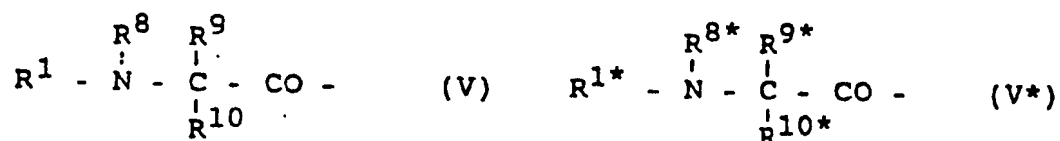


where E, E\*, F, F\*, G and G\*, independent of one another, stand for a natural or an unnatural amino acid, azaamino acid or imino acid;

n, n\*, o, o\*, p and p\*, independent of one another, mean 0 or 1;

D stands for R<sup>1</sup> or a radical of formulas V, VI or VII, and

D\* stands for R<sup>1\*</sup> or a radical of formulas V\*, VI\* or VII\*



and wherein  $R^1$  and  $R^{1*}$ , independent of each other, stand for

$a_1$ )

- hydrogen
- carboxyl.
- $(C_1-C_{18})$ -alkyl, which may be simply or doubly unsaturated and which may be substituted by up to 3 identical or different radicals from the series
- mercapto,
- hydroxy,
- $(C_1-C_7)$ -Alkoxy
- Carbamoyl
- $(C_1-C_8)$ -alkanoyloxy,
- carboxy,
- $(C_1-C_7)$ -alkoxycarbonyl,
- F, Cl, Br, I,
- amino
- amidino, which if appropriate can be substituted by one, two or three  $(C_1-C_8)$ -alkyl radicals,
- guanidino, which if appropriate can be substituted by one or two benzyloxycarbonyl radicals or by one, two, three or four  $(C_1-C_8)$ -alkyl radicals,
- $(C_1-C_7)$ - alkylamino,
- di- $(C_1-C_7)$ -alkylamino,
- $(C_1-C_6)$ -alkoxycarbonylamino,
- $(C_7-C_{15})$ -aralkoxycarbonyl,
- $(C_7-C_{15})$ -aralkoxycarbonylamino,
- [illegible]  $(C_1-C_4)$ -alkoxy

- 9-fluorenylmethoxycarbonylamino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylsulfinyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylthio,
- hydroxamino,
- hydroximino,
- sulfamoyl,
- sulfo,
- carboxamido,
- formyl,
- hydrazono,
- imino,
- a radical CONR<sup>12</sup>R<sup>13</sup> or CONR<sup>12\*</sup>R<sup>13\*</sup>,
- by up to six hydroxy or
- by up to five (C<sub>1</sub>-C<sub>8</sub>)-alkanoxyloxy;
- mono-, bi- or tri-cyclic (C<sub>3</sub>-C<sub>18</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>18</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, the cycloalkyl part in each case being substituted if appropriate by one or two identical or different radicals from the series
- F, Cl, Br, I,
- carboxy,
- carbamoyl,
- carboxymethoxy,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyl,

- (C<sub>1</sub>-C<sub>7</sub>)-alkyloxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylamino-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- di-(C<sub>1</sub>-C<sub>6</sub>)-alkylamino-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- amidino,
- hydroxamino,
- hydroximino,
- hydrazono,
- imino,
- guanidino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxysulfonyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxysulfinyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino
- (C<sub>6</sub>-C<sub>12</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino and
- trifluoromethyl;
- (C<sub>6</sub>-C<sub>14</sub>)-aryl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryloxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl or
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl, wherein the aryl part in each case is substituted if appropriate by one, two or three identical or different radicals from the series
- F, Cl, Br, I,
- hydroxy,
- mono-, di- or tri-hydroxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,

- trifluoromethyl,
- formyl,
- carboxamido,
- mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylaminocarbonyl,
- nitro,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- carboxy,
- carboxymethoxy,
- amino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonylmethoxy,
- carbamoyl,
- sulfamoyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxysulfonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkylsulfonyl,
- sulfo-(C<sub>1</sub>-C<sub>8</sub>)-alkyl! and
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino;
- het,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,

- het-thio-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, where in each case het stands for the radical of a 5- to 7-member monocyclic or 8- to 10-member bicyclic ring system which can be benzannellated, aromatic, partly hydrogenated or completely hydrogenated, which can contain as heteroelements one, two, three or four different radicals from the group N, O, S, NO, SO, SO<sub>2</sub>, which can be substituted with 1 to 6 hydroxy and which, if appropriate, is mono-, di- or tri-substituted as defined for (C<sub>6</sub>-C<sub>14</sub>)-aryl under a<sub>1</sub>) and/or with oxo, or mean a radical NR<sup>12</sup>R<sup>13</sup> or NR<sup>12\*</sup>R<sup>13\*</sup>,

a<sub>2</sub>)

- $$R^{1a}-W \quad (VIII)$$

$$R^{1a*}-W^* \quad (VIII^*)$$

or wherein R<sup>1</sup> and R<sup>1\*</sup>, independent of each other, together with R<sup>11</sup> or R<sup>11\*</sup> and the atoms that carry them form monocyclic or bicyclic, saturated or partly unsaturated ring systems with 5-12 ring members which in addition to carbon can also contain 1 sulfur atom, which may be oxidized to sulfoxide or sulfone;

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- a glycosyl radical, preferably a glucofuranosyl or glucopyranosyl radical, which is derived from naturally occurring aldotetroses, aldopentoses, aldohexoses, ketopentoses, ketohexoses, desoxyaldoses, aminoaldoses and oligosaccharides as well as their stereoisomers;

$R^2$  and  $R^{2*}$

are defined independent of each other like  $R^1$  and  $R^{1*}$  under  $a_1$ ) or  $a_2$ ) or together with  $R^4$  or  $R^{4*}$  and the atoms carrying them form mono- or bicyclic, saturated or partly unsaturated ring systems with 5 to 12 ring members, or together with  $R^3$  or  $R^{3*}$  and the atoms carrying them form cyclic, saturated or partly unsaturated ring systems with 3 to 12 ring members;

$R^3$  and  $R^{3*}$

independent of each other mean

- hydrogen or
- $(C_1-C_3)$ -alkyl;

$R^4$  and  $R^{4*}$  mean

- hydrogen or
- $(C_1-C_8)$ -alkyl;

$R^5$ ,  $R^{5*}$  and  $R^{5**}$

independent of one another mean

- hydrogen,
- hydroxy,
- amino or
- carboxy, or

with  $R^6$ ,  $R^{6*}$  or  $R^{6**}$  together with the carbon atoms carrying these, in each case independent of one another, form a keto group;

$R^6$ ,  $R^{6*}$  and  $R^{6**}$

independent of one another mean

- hydrogen or
- (C<sub>1</sub>-C<sub>6</sub>)-alkyl or

in the case of  $l=0$ , R<sup>6</sup> and R<sup>6\*</sup> can possibly form a common bond;

R<sup>7</sup> means

- hydrogen,
- hydroxy or
- (C<sub>1</sub>-C<sub>6</sub>)-alkyl;

R<sup>8</sup> and R<sup>8\*</sup>

independent of each other mean

- hydrogen or
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl, or together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form mono- or bicyclic, saturated or partly unsaturated ring systems with 5 to 12 ring members;

R<sup>9</sup> and R<sup>9\*</sup>

independent of each other are defined like R<sup>1</sup> or R<sup>1\*</sup> under a<sub>1</sub>), stand for hydroxy or (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy, or together with R<sup>10</sup> or R<sup>10\*</sup> and the atoms carrying these form cyclic, saturated or partly unsaturated ring systems with 3 to 12 ring members;

or

together with R<sup>11</sup> or R<sup>11\*</sup> and the atoms carrying these form a mono- or bicyclic, saturated or partly unsaturated ring system with 5-12 ring members, which in addition to carbon can also contain 1 sulfur atom, which possibly can be oxidized to sulfoxide or sulfone; or can contain 1 nitrogen atom, the ring system possibly being substituted by amino;

R<sup>10</sup> and R<sup>10\*</sup>

- hydrogen or

**R<sup>11</sup> and R<sup>11\*</sup>**

- hydrogen,

- hydroxy,

- (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy or

- (C<sub>1</sub>-C<sub>8</sub>)-alkyl;

 $R^{12}, R^{12*}, R^{13} \text{ and } R^{13*}$ 

independent of one another mean

- hydrogen,

- (C<sub>1</sub>-C<sub>8</sub>)-alkyl which can be substituted by

- amino,

- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino,

- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino,

- mercapto,

- carboxy,

- hydroxy or

- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,

- (C<sub>3</sub>-C<sub>7</sub>)-cycloalkyl,

- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,

- (C<sub>6</sub>-C<sub>14</sub>)-aryl, (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl which in the aryl part can be substituted as described for R<sup>1</sup> or R<sup>1\*</sup>,

- het or

- het-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, het being defined as described for R<sup>1</sup> or R<sup>1\*</sup>,



Azaamino acids are derived from natural or unnatural amino acids, the central building block  $\text{-CHR-}$  or  $\text{CH}_2\text{-}$  being replaced by  $\text{-NR-}$  or  $\text{-NH-}$ .

pyrrolidine-2-carboxylic acid;

**piperidine-2-carboxylic acid;**

**1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid:**

**decahydroisoquinoline-3-carboxylic acid:**

**octahydroquinoline-2-carboxylic acid;**

**decahydroquinoline-2-carboxylic acid:**

octahydrocyclopenta[b]pyrrole-2-carboxylic acid:

**2-aza-bicyclo[2.2.2]octo-3-carboxylic acid;**

**2-azabicyclo[2.2.1]heptane-3-carboxylic acid;**

**2-azabicyclo[3.1.0]hexane-3-carboxylic acid:**

**2-azaspiro[4.4]nonane-3-carboxylic acid:**





Cycloalkyl also means alkyl-substituted radicals such as 4-methoxycyclohexyl or 2,3-dimethylcyclopentyl.

By bicycloalkyl or tricycloalkyl is meant an isocyclic aliphatic, non-aromatic radical which can possibly contain non-symmetrically distributed double bonds and can possibly be substituted with open-chain aliphatic lateral chains. The two or three rings as components of such radicals are condensed or spiro-joined and are joined via a ring C atom or a lateral chain C atom. Examples of these radicals are bornyl-, norbornyl-, pinanyl-, norpinanyl-, caranyl-, norcaranyl-, thujanyl-, adamantyl-, bicyclo(3.3.0)octyl-, bicyclo(4.4.0)decyl-, bicyclo(1.1.0)butyl-, spiro(3.3)heptyl substituents.

If the cycles cited carry more than one substitute, these can stand either cis or trans to one another.

(C<sub>6</sub>-C<sub>14</sub>)-aryl is, for example, phenyl, naphthyl, biphenyl or fluorenyl; preferred are phenyl and naphthyl. The same applied correspondingly to radicals derived therefrom, e. g. aryloxy, aroyl, aralkyl and aralkoxy. By aralkyl is meant an unsubstituted or substituted (C<sub>6</sub>-C<sub>14</sub>)-aryl radical joined to (C<sub>1</sub>-C<sub>6</sub>)-aryl such as benzyl, 1- and 2-naphthylmethyl, although aralky would not be limited to the radicals cited.

Het radicals in the sense of the definition above are pyrrolyl, furyl, thienyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, tetrazolyl, pyridyl, pyrazinyl, pyrimidinyl, indolyl, isoindolyl, indazolyl, phthalazinyl, quinolyl, isoquinolyl, quinoxaliny, quinazolinyl, cinnolinyl,



Compounds of formula (I) containing basic groups, e. g. an amino group or a guanidino group, form salts with inorganic acids such as hydrochloric acid, sulfuric acid or phosphoric acid and with organic carboxylic or sulfonic acids such as acetic acid, citric acid, benzoic acid, maleic acid, fumaric acid, tartaric acid and toluene-p-sulfonic acid.

Likewise preferred are compounds of formula I that are C<sub>2</sub>-symmetrical.

Y stands for a radical of formula II or a radical of formula III;

E, E\*, F, F\*, G and G\*, independent of one another, stand for a natural or unnatural  $\alpha$ -amino acid or  $\alpha$ -imino acid;

independent of each other stand for

- 20

- (C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy,
- carboxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- F,
- amino,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino,
- benzyloxycarbonyl,
- benzyloxycarbonylamino,
- 9-Fluorenylmethoxycarbonylamino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfonyl,
- a radical CONR<sup>12</sup>R<sup>13</sup> or CONR<sup>12\*</sup>R<sup>13\*</sup>,
- by up to six hydroxy or
- by up to four (C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy;
- mono- or bicyclic (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl where in each case the cycloalkyl part is substituted by one or two identical or different radicals from the series
- F,
- carboxy,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyloxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino,

- benzyloxycarbonylamino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino and
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino;
- (C<sub>6</sub>-C<sub>10</sub>)-aryl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryloxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl or
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, wherein the alkyl part in each case is possibly substituted by one, two or three identical or different radicals from the series
- F, Cl, Br,
- hydroxy,
- hydroxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- carboxamido,
- mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylaminocarbonyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- carboxy,
- carbamoyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino;
- het,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-(C<sub>5</sub>-C<sub>6</sub>)-cycloalkyl,
- het-thio-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,

where het in each case stands for a 5- to 6-member monocyclic or 8- to 10-member bicyclic ring system which can be aromatic, partly hydrogenated or completely hydrogenated, which can contain as heteroelements one, two, three or four different radicals from the group N, O, S, NO, SO, SO<sub>2</sub>, which can be substituted with 1 to 4 hydroxy and which can possibly be mono- or di-substituted as defined for (C<sub>6</sub>-C<sub>10</sub>)-aryl under a<sub>1</sub>) and/or with oxo, or means a radical NR<sup>12</sup>R<sup>13</sup> or NR<sup>12\*</sup>R<sup>13\*</sup> or,

$$R^{1a} - W \quad (VIII)$$

wherein  $R^{1a}$  and  $R^{1a*}$  are defined like  $R^1$  and  $R^{1*}$  under a<sub>1</sub>) and W or W\* stand for -CO-, -O-CO-, -SO<sub>2</sub>-, -SO-, -S-, -NHCO- or -CH(OH)-;

a<sub>3</sub>) - a glycol radical that is defined as above:

independent of each other mean

- carboxy,

**-hydroxy,**









R<sup>14</sup> stands for

- hydrogen or
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

as well as their physiologically tolerated salts.

Particularly preferred are compounds of formula I in which  
Y stands for a radical of formula II or a radical of formula III;  
l, m, A, A\*, D, D\*, n, n\*, o, o\* are defined as above, p and p\* stand for 1;  
R<sup>1</sup> and R<sup>1\*</sup>

independent of each other stand for

- hydrogen,
- carboxyl,
- (C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<)<)-i)-i)-i)-i)-i)-i),i)-i)-i alkI),I
- phenyl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl, which in the phenyl part can be substituted as described on pages 19/20,
- possibly protected mono- or di-amino-(C<sub>1</sub>-C<sub>12</sub>)-alkyl or amino-(C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl or amino-(C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, such as -2-amino-3-phenyl-propyl,
- mono-, di-, tris-, tetra-, penta- or hexahydroxy-(C<sub>1</sub>-C<sub>10</sub>)-alkyl or -alkanoyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>16</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkylsulfinyl,
- mono-, di-, trihydroxy-(C<sub>1</sub>-C<sub>8</sub>)-alkylsulfonyl,
- mono-, di-, trihydroxy-(C<sub>1</sub>-C<sub>8</sub>)-alkylsulfinyl,

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- (C<sub>1</sub>-C<sub>8</sub>)-alkyl, which is possibly substituted by up to 2 identical or different radicals from the series
- hydroxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylthio,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfinyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy,
- carboxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- amino,
- amidino,
- guanidino,
- N,N'-di-(benzyloxycarbonyl)-guanidino,
- carbamoyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkoxycarbonyl,
- (C<sub>1</sub>-C<sub>5</sub>)-alkoxycarbonylamino,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkoxycarbonylamino, or
- (C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>10</sub>)-cylcoalyl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl, the aryl part possibly being substituted by one, two or three identical or different radicals from the series
- F, Cl, Br,
- hydroxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,

- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl and
- amino, or
- het-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, het being defines as for R<sup>1</sup> or R<sup>1\*</sup>,

### $R^3$ and $R^{3*}$

independent of each other mean

- hydrogen or

- methyl,

### $R^4$ and $R^{4*}$

independent of each other mean

- hydrogen or

- methyl,

 $R^5, R^{5^*}$  and  $R^{5^{**}}$ 

independent of one another mean

- hydrogen,

- hydroxy,

- amino or

- carboxy;

**R<sup>6</sup>, R<sup>6\*</sup> and R<sup>6\*\*</sup>**

independent of one another mean

- hydrogen or

- methyl;

**R<sup>7</sup> means**

- hydrogen,

- hydroxy or

- methyl;

independent of each other mean

- methyl, ethyl or n-propyl, or together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form a 1,2,3,4-tetrahydroisoquinoline or a 2-azabicyclooctane skeleton;

independent of each other are defined like  $R^2$  and  $R^{2*}$  on pages 27/28 or mean  $(C_1-C_8)$ -alkanoyloxy or

together with  $R^{10}$  or  $R^{10*}$  and the atoms carrying these form cyclic ring systems with 5 to 7 ring members;

or together with R<sup>11</sup> or R<sup>11\*</sup> form a form a thiochroman system the sulfur atom of which can if appropriate be oxidized to sulfone;

independent of each other mean

- methyl;

$R^{11}$  and  $R^{11*}$  are defined as on page 24;

in the aforementioned compounds of formula I one or more amide groups (-CONH-) of the main chain can be replaced as defined n page 24;

- hydrogen or

- methyl;

as well as their physiologically tolerated salts.

Also preferred are compounds of formula I in which

independent of each other stand for

-

-

- 

- benzylfulfinyl or
- 4-chlorobenzylthio,
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,
- (C<sub>1</sub>-C<sub>12</sub>)-alkanoyl which is substituted by hydroxy, amino and possibly by phenyl or cyclohexyl, such as
- 2-amino-1-hydroxy-4-methyl-pentyl,
- possibly protected, amino-substituted (C<sub>6</sub>-C<sub>10</sub>)-aryl- or (C<sub>3</sub>-C<sub>10</sub>)-alkyl or (C<sub>1</sub>-C<sub>8</sub>)-alkyl, such as
- 2-amino-3-phenyl-propyl or
- N-tert.-butoxycarbonyl-2-amino-3-phenyl-propyl,
- (C<sub>1</sub>-C<sub>10</sub>)-alkoxycarbonyl, such as
- methoxycarbonyl,
- ethoxycarbonyl,
- isobutoxycarbonyl or
- tert.-butoxycarbonyl,
- substituted (C<sub>1</sub>-C<sub>10</sub>)-alkoxycarbonyl, such as
- 2-(trimethylsilyl)-ethoxycarbonyl,
- 2,2,2-trichloroethoxycarbonyl or
- 1,1-dimethyl-2,2,2-trichloroethoxycarbonyl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonyl, such as
- benzyloxycarbonyl,
- 1- or 2-naphthylmethoxycarbonyl or
- 9-fluorenylmethoxycarbonyl,
- 1-deoxyhexoketosyl or 1-deoxypentoketosyl, such as
- 1-deoxyfructos-1-yl, 1-deoxysorbos-1-yl or 1-deoxyribulos-1-yl

- hexosyl or pentosyl, such as
- mannosyl, glucosyl or galactosyl,
- xylosyl, ribosyl or arabinosyl,
- 6-deoxyhexosyl, such as
- rhamnosyl, fucosyl or deoxyglucosyl,
- amino sugar radicals, such as
- 2-amino-2-deoxyglucosyl,
- 2-acetamido-2-deoxyglucosyl,
- 2-amino-2-deoxygalactosyl or
- 2-acetamido-2-deoxygalactosyl,
- lactosyl,
- maltosyl,

it being possible for the joined sugar to be present in the pyranose or furanose form,

- het, such as
- 2-pyridyl,
- 4-pyridyl,
- 2-(N-oxidopyridyl) or
- 4-(N-oxidopyridyl),
- het-carbonyl or het-sulfonyl, such as
- piperidino-4-carbonyl,
- morpholino-4-carbonyl,
- pyrrolyl-2-carbonyl,
- pyridyl-3-carbonyl,
- quinolyl-2-carbonyl
- 4-tert.-butoxycarbonylamino-1-piperidylcarbonyl,

- 4-amino-1-piperidylcarbonyl,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, such as
- 2-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- 3-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl or
- 4-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkanoyl or het-(C<sub>1</sub>-C<sub>6</sub>)-alkylsulfonyl, such as
- 2-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkanoyl,
- 3-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkanoyl,
- 4-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkanoyl,
- 2-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkylsulfonyl,
- 3-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkylsulfonyl or,
- 4-pyridyl-(C<sub>1</sub>-C<sub>6</sub>)-alkylsulfonyl,
- het-mercapto-(C<sub>1</sub>-C<sub>3</sub>)-alkylcarbonyl, such as
- 2-pyridylthioacetyl,

- pyrrolyl,
- imidazolyl,
- pyridyl,
- pyrimidyl,
- pyrrolidyl,
- piperidyl,
- morpholino,
- quinolyl or
- isoquinolyl,

$R^2$  and  $R^{2*}$ 

- hydrogen,
- carboxyl,
- methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec.-butyl, n-pentyl, n-hexyl,
- cyclohexyl,
- cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl,
- 4-methylcyclohexylmethyl,
- 1-decahydronaphthylmethyl, 2-decahydronaphthylmethyl,
- phenyl,
- benzyl,
- 2-phenylethyl,
- 1-naphthylmethyl, 2-naphthylmethyl,
- 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl,
- 2,4,6-trimethylbenzyl,
- 4-tert.-butylbenzyl,
- 4-tert.-butoxybenzyl
- 4-hydroxybenzyl,
- 4-methoxybenzyl,
- 2,4-dimethoxybenzyl,
- 3,4-dihydroxybenzyl,
- 3,4-dimethoxybenzyl,



**R<sup>7</sup> means**

- methyl;

 $R^8$  and  $R^{8*}$ 

independent of each other mean

- hydrogen or

together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form a 1,2,3,4-tetrahydroisoquinoline or 2-azabicyclooctane skeleton;

**R<sup>9</sup> and R<sup>9\*</sup>**

independent of each other are defined like  $R^2$  or  $R^{2*}$  or mean

- hydroxy,

- acetoxy,

- tert.-butoxymethyl,

- 3-guanidinopropyl,

- carbamoylmethyl, carbamoylethyl,

- carboxymethyl, carboxyethyl,

- mercaptomethyl,

- (1-mercapto-1-methyl)ethyl,

- aminomethyl, 2-aminoethyl, 3-aminopropyl, 4-aminobutyl,

- N,N-dimethylamino,

- N,N'-di-(benzyloxycarbonyl)-guanidino-propyl,

- 2-benzyloxycarbonyl ethyl, benzyloxycarbonylmethyl,

- tert.-butylsulfonylmethyl

or

- 4-benzylcarbonylaminobutyl;

independent of each other mean

- and in the aforementioned compounds of this invention one or more amide groups (-CONH-) of the main chain can be replaced by -CH<sub>2</sub>NR<sub>14</sub>- or -CH(OH)CH<sub>2</sub>-;

- hydrogen or
- methyl;

Very particularly preferred are compounds of formula I wherein R<sup>1</sup> and R<sup>1\*</sup>

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- benzolsulfonyl, -sulfinyl or - thio possibly substituted by halogen, amino, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or methoxy, such as
- 4-chlorobenzylsulfonyl,
- benzylsulfinyl or
- 4-chlorobenzylthio,
- het, such as
- 2- or 4-pyridyl or
- 2- or 4-(N-oxidopyridyl),
- het-sulfonyl, such as
- 4-tert.-butoxycarbonylamino-1-piperidylsulfonyl or
- 4-amino-1-piperidylsulfonyl,
- het-(C<sub>1</sub>-C<sub>4</sub>)-alkylsulfonyl, such as
- 2-(4-pyridyl)-ethylsulfonyl,
- het-(C<sub>1</sub>-C<sub>4</sub>)-alkanoyl, such as
- 2-pyridylacetyl,
- 3-pyridylacetyl,
- 4-tert.-butoxycarbonylamino-1-piperidylcarbonyl,
- 4-amino-1-piperidylcarbonyl or
- 2-quinolylcarbonyl,
- het-mercapto-(C<sub>1</sub>-C<sub>3</sub>)-alkylcarbonyl, such as
- 2-pyridylthioacetyl,

- pyrrolyl,
- imidazolyl,
- pyridyl,
- pyrimidyl,

- pyrrolidyl,
- quinolyl,
- isoquinolyl,
- piperidyl or
- morpholino,

it also being possible that this radical is substituted by one or two identical or different radicals from the group methyl, amino and (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,

- amino-(C<sub>3</sub>-C<sub>6</sub>)-cycloalkylcarbonyl, such as

- 2-aminocyclopropylcarbonyl,

- 3-aminocyclobutylcarbonyl,

- 3-aminocyclopentylcarbonyl,

- 4-aminocyclohexylcarbonyl,

- (C<sub>1</sub>-C<sub>8</sub>)-alkanoyl, which is substituted by hydroxy and amino and possibly by phenyl or cyclohexyl, such as

2-amino-1-hydroxy-4-methyl-pentyl-

- possibly protected amino-substituted phenyl- or cyclohexyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,  
such as

- 2-amino-3-phenyl-propyl or

- N-tert.-butoxycarbonyl-2-amino-3-phenyl-propyl,

- amino,

- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,

- benzyloxycarbonylamino,

- 1-deoxyhexoketosyl or 1-deoxypentoketosyl, such as

- 1-deoxyfructos-1-yl, 1-deoxysorbos-1-yl or

- 1-deoxyribulos-1-yl,

- hexosyl or pentosyl, such as
- mannosyl, glucosyl or galactosyl, or
- xylosyl, ribosyl or arabinosyl, it being possible for the joined sugar to be present in the pyranose or the furanose form,

- hydrogen,
- methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec.-butyl, pentyl, hexyl,
- cyclopentylmethyl, cyclohexylmethyl,
- 4-methylcyclohexylmethyl,
- benzyl,
- 2-phenylethyl,
- 1-naphthylmethyl, 2-naphthylmethyl,
- 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl,
- 2,4,6-trimethylbenzyl,
- 4-tert.-butylbenzyl,
- 4-methoxybenzyl,
- 3,4-dihydroxybenzyl,
- 2,4-dimethoxybenzyl,
- 3,4-dimethoxybenzyl,
- 3,4-dimethylenedioxybenzyl,
- 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl or
- 2-(4-pyridyl)ethyl;

**R<sup>3</sup>, R<sup>3\*</sup>, R<sup>4</sup>, R<sup>4\*</sup>, R<sup>6</sup>, R<sup>6\*</sup>, R<sup>7</sup>, R<sup>10</sup> AND R<sup>10\*</sup>**

mean hydrogen;

independent of each other mean

- hydrogen or
- hydroxy;

$R^8$  and  $r^{8*}$  independent of each other are defined as on page 36,

**R<sup>9</sup> and R<sup>9\*</sup>**

independent of each other are defined like  $R^g$  and  $R^{g*}$  on page 36;

$R^{11}$  and  $R^{11*}$  independent of each other are defined as on page 37.

as well as their physiologically tolerated salts.

Also preferred in particular are compounds of formula I in which Y stands for a radical of formula III;

1 means 0 or 1;

m means 1;

$A$ ,  $A^*$ ,  $D$  and  $D^*$  are defined as above;

$n, n^*, o, o^*, p$  and  $p^*$  independent of one another mean 1;

E, E\*, F, F\*, G and G\* independent of one another stand for an amino acid from the series Val, Lys, Lys(Z), Phe, Chg, Ser, Asn, Gly, Ile, Tbg, Nva or Npg;

$R^1$  and  $R^{1*}$  independent of each other mean

- hydrogen,
- carboxyl,
- methylsulfonyl,
- tert.-butylsulfonyl,
- tert.-butoxycarbonyl,
- 2-hydroxyethylsulfonyl,
- 1,2,3-trihydroxypropyl,
- 1,2,3-triacetoxypentyl,

- benzyloxycarbonyl,
- 4-methylphenylsulfonyl,
- 4-chlorobenzylthio,
- benzylsulfinyl,
- 4-chlorobenzylsulfonyl,
- hexadecylsulfonyl,
- 4-amino-1-piperidyl-sulfonyl,
- N-tert.-butoxycarbonyl-4-amino-1-piperidyl-sulfonyl,
- 4-amino-1-piperidyl-carbonyl,
- N-tert.-butoxycarbonyl-4-amino-1-piperidyl-carbonyl,
- 2-amino-3-phenyl-propyl,
- N-tert.-butoxycarbonyl-2-amino-3-phenyl-propyl,
- 2-amino-1-hydroxy-4-methyl-pentyl,
- deoxyfructos-1-yl,
- mannofuranosyl,
- 4-aminocyclohexylcarbonyl,
- 2-quinolylcarbonyl,
- 1-naphthylacetyl,
- 1-naphthyloxyacetyl,
- 1-(4-pyridyl)-ethylsulfonyl,
- 12-aminododecanoyl,
- 4-(N-oxidopyridyl),
- 4-pyridyl,
- tetradecanoyl,
- 2-pyridylacetyl,
- 4-pyridylthio-acetyl,

- phenyl,
- amino or
- tert.-butoxycarbonylamino;

$R^2$  and  $R^{2*}$  independent of each other mean

- hydrogen,
- 2-(4-pyridyl)ethyl,
- isopropyl,
- isobutyl,
- n-pentyl,
- benzyl,
- 3,4-methylenedioxybenzyl,
- 2,4-dimethoxybenzyl,
- 4-tert.-butylbenzyl,
- 2-phenylethyl or
- cyclohexylmethyl;

**R<sup>3</sup>, R<sup>3\*</sup>, R<sup>4</sup>, R<sup>4\*</sup>, R<sup>6</sup>, R<sup>6\*</sup>, R<sup>7</sup>, R<sup>10</sup> and R<sup>10\*</sup> mean**

- hydrogen;

$R^5$  and  $R^{5*}$  independent of each other mean

- hydrogen or
- hydroxy;

$R^8$  and  $R^{8*}$  mean

- hydrogen, or together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form a 1,2,3,4-tetrahydroquinoline-3,4-diyl system;

$R^9$  and  $R^{9*}$  independent of each other mean

- hydrogen,
- hydroxy,





-



$R^3, R^{3*}, R^4, R^{4*}, R^6, R^{6*}, R^{11}$  and  $R^{11*}$  mean

**R<sup>5</sup> and R<sup>5\*</sup> mean hydroxy;**

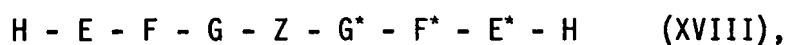
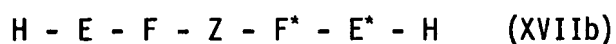
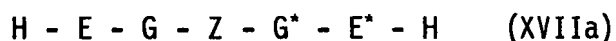
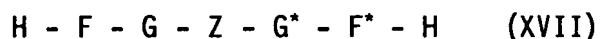
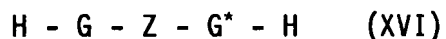
The present invention furthermore concerns a process for the preparation of compounds of formula (I) characterized in that a fragment with terminal carboxyl group or its reactive derivative is coupled to a corresponding fragment with free amino group, for protection of other functional groups a temporarily inserted protective group(s) is split off and the compound thus obtained is, if appropriate, converted into its physiologically tolerated salt.

$$D - OH \quad (VIII)$$
$$\text{D} - \text{E} - \text{OH} \quad (\text{IX})$$

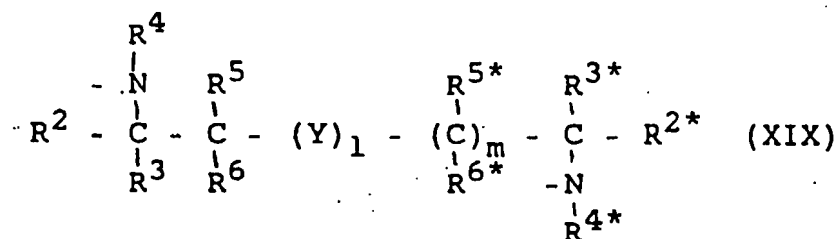
D - F - OH (X)

$$\text{D} - \text{G} - \text{OH} \quad (\text{XI})$$
$$D - E - F - OH \quad (XII)$$
$$\text{D} - \text{E} - \text{G} - \text{OH} \quad (\text{XIII})$$
$$D - F - G - OH \quad (XIV)$$
$$\text{D} - \text{E} - \text{F} - \text{G} - \text{OH} \quad (\text{XIVa})$$

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$$\text{H} - \text{Z} - \text{H} \quad (\text{XV})$$


Z standing for a radical of formula (XIX):



Methods suitable for producing an amide bond are described, for example, in Houben-Weyl, Methoden der organischen Chemie (Methods of Organic Chemistry), vol. 15/2; Bodanszky, et al., Peptide Synthesis, 2nd ed. (Wiley & Sons, New York 1976) or Gross, Meienhofer, The Peptides: Analysis, synthesis, biology (Academic Press, New York 1979). Preferably the following methods are used: active ester method with N-hydroxy-succinimide, 1-hydroxybenzo-triazole or 3-hydroxy-4-oxo-3,4-dihydro-1,2,3-benzotriazine as alcohol component,

coupling with a carbodiimide such as dicyclo-hexylcarbodiimide (DCC) or with n-propanephosphonic anhydride (PPA) and the mixed-anhydride method with pivaloylchloride or chloroformic ethyl ester or -isobutyl ester, or coupling with phosphonium reagents such as benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (BOP) or uronium reagents such as 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoro-borate (TBTU).

Fragments of formula (VIII) or (VIII\*) if they fall under

- a) formula (V) or (V\*) are synthesized according to the general methods for the preparation of amino acids;
- b) formula (VI) or (VI\*) are synthesized, for example, proceeding from the corresponding amino acids, their chirality center being preserved. Diazotizing at -20°C to 50°C in dilute mineral acids leads to  $\alpha$ -bromocarboxylic acid or via the lactic acids to  $\alpha$ -trifluoromethanesulfonyloxy carboxylic acid which can be reacted with a nucleophile bearing an R<sup>1</sup> and R<sup>11</sup> or R<sup>1\*</sup> and R<sup>11\*</sup>, or are prepared, for example, proceeding from malonic esters, the alkylation of which produces mono- or di-substituted malonic esters which, after saponification by decarboxylation, are converted into the desired derivatives.
- c) Formula (VII) or (VII\*) are synthesized proceeding from the corresponding  $\alpha$ -amino acids, their chirality center being preserved. Diazotizing at -20°C to 50°C in dilute mineral acids leads to lactic acids which can be reacted with an electrophile bearing R<sup>1</sup> or R<sup>1\*</sup>.

Fragments of formulas (IX), (X), (XI), (XII) and (XIII), (XIV) and (XIVa) are synthesized according to the generally known methods for the preparation of amino acids and peptides.

Fragments of formula (XV) are synthesized proceeding from optically active  $\alpha$ -amino acids or sugars or their derivatives. For example, for the preparation of fragments with  $m = 1$ ,  $l = 0$ ,  $R^5 = R^{5*} = OH$  and  $R^6 = R^{6*} = H$  the amino acids are converted in known manner into N-protected amino acid aldehydes (B. Castro, et al., Synthesis 1983, 676) and reductively reacted with suitable metals, metallic salts, or also electrochemically to N-protected diaminodiols. For this, for example, the N-protected aldehydes are dissolved in tetrahydro-furan and at  $-30^\circ C$  to  $60^\circ C$ , preferably  $-10^\circ C$  to  $30^\circ C$  are converted into the N-protected diaminodiols by the addition of a solution of samarium(II) iodide in tetrahydrofuran.

With synthesis from sugar (derivATIVES) the chirality centers of the initial material are preserved or inverted. OH groups that are to be preserved are protected in suitable manner; the others are activated by reaction with, for example, a sulfonic acid chloride or according to MitsunOBU (Synthesis (1981), 1-28) and can be exchanged by nucleophiles. The desired products are obtained here in stereochemically uniform form.

Proceeding, for example, from D-mannitol the hydroxy groups of the polyol in positions 3 and 4 are protected by treatment with acetone/sulfuric acid and subsequently with aqueous acetic acid as acetone. By reaction of the two terminal OH groups with p-toluenesulfonyl chloride/pyridine and treatment with potassium carbonate in methanol one obtains the 1,2R-5R,6-diepoXide-3,4-O-isopropylidene-3R,4R-diol (Y. Le Merrer, et al., Tetrahedron Lett. 26 z(1985) 319-322). Treatment of the diepoXide with cuprates in, for

Fragments of formula (XV) with  $m = 1$ ,  $l = 1$  and  $Y =$  radical of formula III are obtained in such a manner that N-protected amino acid aldehydes (see above) are reacted under reductive conditions (e.g.  $\text{NaBH}_3\text{CN}$ ) with a suitable amine.

Fragments of formula XV with  $m = 0$ ,  $l = 0$ ,  $R^5 = OH$ ,  $R^6 = H$  are obtained in such a manner that suitable nitro compounds are deprotonated with bases such as tetramethylguanidine and added to N-protected amino acid aldehydes (see above). Reduction of the nitro group with, for example, Raney nickel and splitting off the protective groups yields the compounds of formula (XV) as diastereomers which are separated as described above.

In the compounds of formula I one or more amide groups can be replaced by  $-\text{CH}_2\text{NR}^{14}-$ ,  $-\text{CH}_2\text{S}-$ ,  $-\text{CH}_2\text{O}-$ ,  $\text{OCH}_2-$ ,  $-\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}=\text{CH}-$  (cis and trans),  $-\text{COCH}_2-$ ,  $-\text{CH}(\text{OH})\text{CH}_2-$ ,  $-\text{CH}_2\text{SO}-$ ,  $-\text{CH}_2\text{SO}_2-$ ,  $-\text{COO}-$ ,  $-\text{P}(\text{O})(\text{OR}^{15})\text{CH}_2-$ ,  $-\text{P}(\text{O})(\text{OR}^{15})_2\text{NH}-$  or  $-\text{NH}-\text{CO}-$ .



The compounds of formula I according to the invention exhibit enzyme-inhibiting properties. In particular, they inhibit the action of retroviral aspartyl proteases such as those of the HIV proteases. Their enzyme-inhibiting effect, which lies in the milli- to subnano-molar range, can be determined as follows.

Among others, the heptapeptide H-Ser-Phe-Asn-Phe-Pro-Gin-Ile-OH (P. L. Darke, et al., Biophys. Res. Commun. 156 (1988) 297-303) has been used as substrate of the HIV protease. The HIV protease splits the substrate between the second Phe and Pro.

## General instructions for the testing of inhibitors of HIV proteases

2 mg H-Ser-Phe-Asn-Phe-Opr-Gln-Ile-OH (H-Opr-OH = 5-oxaproline) are dissolved in 1 ml MGTE-15 buffer (possible use of ultrasound) and then filtered via a sterile filter (0.45  $\mu$ m).

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Of the inhibitor, 2.5 times the desired molarity per ml solution are weighed and dissolved with DMSO (10% of the final volume). The solution is diluted with MGTE-15 buffer up to the final volume and filtered via sterile filter (0.45  $\mu$ m).

c) Preparation of the protease solution:

5  $\mu$ l of the HIV protease solution are diluted as needed with MGTE25 buffer.

d) Test performance:

10  $\mu$ l of the substrate solution are pipetted into each test tube (16 x 100) with screw-cap. For the blind test 10  $\mu$ l MGTE15 buffer containing 10% DMSO are pipetted. 10  $\mu$ l each of the inhibitor solutions are added to the remaining test tubes. The solutions are incubated for 5-10 minutes at 37°C and 5  $\mu$ l of the protease solution are then added to each sample. After 2 hours of reaction at 37°C 10 or 20  $\mu$ l (depending on the sensitivity of the HPLC equipment) are pipetted off from each sample, poured into microvials and diluted with 120  $\mu$ l of the HPLC mobile solvent.

e) Conditions for the HPLC analysis:

Mobile solvent system: 80% 0.1 M phosphoric acid pH 2.5  
20% (w/w) acetonitrile

column: Merck LICHROSORB RP18 (5  $\mu$ m) 250x4

flow: 1 ml/min

temperature of the column: 42°C

detector parameters: 215 nm, 0.08 AUF, 18.2°C

analysis time: 11 minutes

retention time of the substrate: 8.1 minutes

retention time of the N-terminal tetrapeptide: 3.9 minutes.



g) Evaluation:

Under the conditions selected here the heptapeptides separate from the N-terminal tetrapeptide resulting from enzymatic splitting. The % content of the tetrapeptide peak with reference to sum tetrapeptide + heptapeptide corresponds to the splitting rate. The subsequent  $IC_{50}$  values indicate at which inhibitor concentration the splitting rate is halved.

Example no.	IC <sub>50</sub>	Example no.	IC <sub>50</sub>
1	10 nm	18	1.2 nm
5	3.6 nm	19	0.7 nm
6	8.8 nm	21	220 nm
7	18 nm	25	18 μm
8	30 μm	28	3 μm
10	17 nm	30	30 nm
11	0.8 nm	33	20 μm
13	1.3 nm	39	1.3 nm
14	1.0 nm	40	13 nm
15	400 nm	43	1.0 nm
16	0.85 nm	45	1.5 μm
17	0.85 nm	48	80 μm



The target peptide was built up in steps with a peptide synthesizer Model 430 A by the firm of Applied Biosystems using the Fmoc method on a p-benzyloxybenzylalcohol resin esterified with Fmoc-Ile-OH from the firm of Novabiochem (charge about 0.5 mmol/g resin). 1 g of the resin was used and the synthesis was carried out with the aid of synthesis program modified for the Fmoc method.

The following amino acid derivatives are used: Fmoc-Gln-OH, Fmoc-Opr-OH, Fmoc-Phe-OObt, Fmoc-Asn-OH and Fmoc-Ser(tBu)-OObt. For the synthesis of Fmoc-Opr-OH, H-Opr-OtBu was synthesized according to the method of Vasella, et al. (J. C. S. Chem. Comm. 1981, 97-98) and reacted with Fmoc-OSu in dioxane/water (1:1) in the presence of  $\text{NaHCO}_3$ . The subsequent splitting of the tert.-butylester with trifluoroacetic acid produces Fmoc-Opr-OH.

In each case 1 mmol of the amino acid derivatives with free with free at free the free the free the free the free the free the free the groupin group group with a free. groupin group group with a free. groupin group's. free.. the the..................... In each case 1 mmol of the amino acid derivatives with free carboxyl group together with 0.95 mmol HOOBt was weighed into the cartridges of the synthesizer. The preactivation of these amino acids was accomplished directly in the cartridges by dissolving in 4 ml DMF and addition of 2 ml of a 0.55 molar solution of diisopropylcarbodiimide in DMF. The HOOBt esters of the other amino acids were dissolved in 6 ml NMP and then like the in situ preactivated amino acids were coupled to the resin previously deblocked with 20% piperidine in DMF. At the conclusion of the synthesis the peptide was then split off from the resin with simultaneous removal of the lateral-chain protective groups using thioanisole and ethanedithiol as cation trap. The residue obtained after withdrawing the trifluoroacetic acid was digested several times with acetic ester and centrifuged.

The remaining residue was chromatographed on an alkylated dextran gel with 10% acetic acid. The fraction containing the pure peptide was combined and freeze-dried.

Mass spectrum (FAB): 854 ( $M + H^+$ )

Amino acid analysis Asp: 0.98; Ser: 0.80; Glu: 1.00; Ile: 1.05; Phe: 2.10;  $NH_3$ : 1.76.

The invention also concerns the use of the compounds of formula I as drugs and pharmaceutical preparations that contain these compounds. Use in primates, especially humans, is preferred.

Pharmaceutical preparations contain an effective amount of the effective substance according to formula I together with an inorganic or organic pharmaceutically usable carrier substance. Application can be intranasal, intravenous, subcutaneous or peroral. Dosing of the effective substance depends on the homoiotherm species, the body weight, age and on the type of application.

The pharmaceutical preparations of the present invention are produced in known dissolving, mixing, granulating or coating processes.

For an oral application form the active compounds are mixed with the usual additives such as carrier substances, stabilizers or inert diluents, and brought into suitable administration forms such as tablets, coated pills, insert capsules, aqueous, alcoholic or oily suspensions or aqueous, alcoholic or oily solutions. As inert carriers it is possible to use, for example, gum arabic, magnesia, magnesium carbonate, potassium phosphate, lactose, glucose, magnesium stearyl fumarate or starch, especially corn starch. The preparation! can be accomplished as dry or moist granulate. Oleaginous carriers can be, for example, animal or vegetable oils such as sunflower oil or cod-liver oil.

Likewise possible is the use of injectable delayed-release preparations. As drug forms it is possible to use, for example, oleaginous crystal suspensions, microcapsules, rods or implants. The latter two can be of tissue-compatible polymers, especially biodegradable polymers such as those on the basis of polylactic acid-polyglycolic acid copolymers or human albumin.

## Chg: cyclohexylglycyl

**D:** doublet

**DCC:** dicyclohexylcarbodiimide

DMF: dimethylformamide

DMAP: 4-dimethylaminopyridine

**DMSO:** dimethyl sulfoxide

EDAC: 1-(3-dimethylamino-propyl)-3-ethyl-carbodiimide hydrochloride

EA: ethyl acetate

FAB: fast atom bombardment

**HOBt:** hydroxybenzotriazole

i. vac.: in a vacuum

m: multiplet

M: molecular peak

NEM: N-ethylmorpholine

Npg: neopentylglycyl

MS: mass spectroscopy

PPA: n-propylphosphonic anhydride

RT: room temperature

s: singlet

m.p.: melting point

t: triplet

Tbg: tert.-butylglycyl

TBTU: 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate

THF: tetrahydrofuran

Thia: 2-thienylalanyl

Z: benzyloxycarbonyl

The other abbreviations used for amino acids correspond to the three-letter code customary in peptide chemistry (as described, for example, in Eur. J. Biochem. 138 (1984), 9-37. Unless expressly stated otherwise, an amino acid of the L configuration is always involved.

The following examples serve to explain the present invention without restricting it.

### Example 1

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

100 mg N,N'-bis-(L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride together with 111 mg N-tert.-butoxycarbonyl-L-phenylalanine, 0.57 ml NEM and 60 mg HOBt were dissolved in 1.5 ml DMF. After addition of 85 mg EDAC at 0°C the solution was stirred further for 1 h at 0°C and then overnight at RT. The solvent was spun off i. vac., the residue was taken up in EA and extracted with saturated  $\text{KHCO}_3$ -10%  $\text{KHSO}_4$  solution and water. The organic phase was dried with anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was recrystallized from ethanol-water.

The yield was 92 mg.

MS (FAB): 993 (M + H)<sup>+</sup>, 975, 893, 793

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.72 (d, 6 Hz, 6H); 0.75 (d, 6Hz, 6H); 1.29 (s, 18H); 1.86 (m, 2H); 2.60-2.96 (m, 8H); 3.30 (m, 2H); 4.17 (m, 2H); 4.45 (m, 2H); 4.68 (m, 2H); 7.03 (d, 9Hz, 2H); 7.05-7.30 (m, 22H); 7.53 (d, 9Hz, 2H).

## Example 2

N,N'-bis-(L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol-dihydrochloride

220 mg N,N'-bis-(tert.-butoxycarbonyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-3,4-O-isopropylidene-hexane-3R,4R-diol in 10 ml of an approximately 3N solution of HCl in dioxane/methanol 1/1 were stirred for 1 h at RT. The volatile components of the solution were removed i. vac. and drying was accomplished in a high vacuum. The substance was used in the next step without further refining.

Yield: 184 mg

MS (FAB): 499 (M + H)<sup>+</sup>, 481, 463

N,N'-bis-(tert.-butoxycarbonyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-3,4-O-isopropylidene-hexane-3R,4R-diol

The yield was: 230 mg

MS (FAB): 739 (M + H)<sup>+</sup>, 681, 639, 569, 539

**2S,5S-diamino-1,6-diphenyl-3,4-O-isopropylidene-hexane-3R,4R-diol**

**Yield:** 1.33 g

MS (FAB): 341 (M + H)<sup>+</sup>

NMR (270 MHz; DMSO  $\langle D_6 \rangle$ ): 1.29 (m, 4H), 1.37 (s, 6H); 2.71 (dd, 12Hz, 5 Hz, 2H); 2.87 (m, 2H); 3.32 (m, 2H); 3.95 (s, 2H); 7.12-7.33 (m, 10H)

2S,5S-diazido-1,6-diphenyl-3,4-O-isopropylidene-hexane-3R,4R-diol

8.5 g 2R,5R-di-(4-nitrophenylsulfonyloxy)-1,6-diphenyl-3,4-O-isopropylidene-hexane-3S,4S-diol were dissolved in 300 ml DMF and heated with about 9.2 g NaN<sub>3</sub> and 6.3 g 18-Krone-6 for 4 h at 50°C. Most of the solvent was spun off i. vac., the residue was taken up in ether and extracted with aqueous NaHCO<sub>3</sub> solution. After washing with water the solution was dried and concentrated. The residue was chromatographed on silica gel (toluene/n-heptane 2/5 to 2/3).

**Yield:** 2.37 g

NMR (270 MHz, DMSO  $d_6$ ): 1.48 (s, 6H); 2.92-3.12 (m, 4H); 3.74 (dd, 10 Hz, 5 Hz, 2H); 4.15 (s, 2H); 7.21-7.39 (m, 10H)

### Example 2d

**2R,5R-di-(4-nitrophenylsulfonyloxy)-1,6-diphenyl-3,4-O-isopropylidene-hexane-3S,4S-diol**

5.6 g 2R,5R-dihydroxy-1,6-diphenyl-3,4-O-isopropylidene-hexane-3R,4R-diol together with 7.9 g DMAP were dissolved in 300 ml chloroform. 14.5 g p-nitrobenzenesulfonyl chloride were added at RT and the solution was stirred for 3 h at 50°C. Methylene chloride was added and the solution was extracted with bicarbonate, KHSO<sub>4</sub> and NaCl solution. After drying of the organic phase it was concentrated.

**Yield: 11.8 g**

MS (FAB): 713 (M + H)<sup>+</sup>, 697, 510

NMR (270 MHz, DMSO  $\text{d}_6$ ): 1.42 (s, 6H); 2.87 (dd, 15Hz, 9Hz, 2H); 3.11 (dd, 15Hz, 3Hz, 2H); 4.41 (s, 2H), 5.07 (dm, 9Hz, 2H), 6.95-7.11 (m, 10H); 7.73 (d, 9Hz, 4H); 8.18 (d, 9Hz, 4H)

### Example 2e

**2R,5R-dihydroxy-1,6-diphenyl-3,4-O-isopropylidene-3R,4R-diol**

Under argon, 1.12 g 1,2R-5R,6-diepoxy-3,4-O-isopropylidene-3R-4R-diol (Y. Le Merrer, A. Dureault, C. Gravier, D. Languin and J. C. Depeyay, Tetrahedron Lett. 26 (1985) 319-322) were added at -78°C to a solution of 36 mmol (C<sub>6</sub>-H<sub>5</sub>)<sub>2</sub>CuLi in 60 ml dry ether. The cold bath was removed and the solution was permitted to warm to RT with stirring. 250 ml EA were added to the solution and it was extracted three times with a mixture of 25% ammonia and ammonium chloride. The EA phase was washed with NaCl solution, dried and concentrated. The residue was refined over silica gel (dichloro-methane/EA 97/3 to 90/10).

**Yield:** 1.86 g

MS (FAB): 343 (M + H)<sup>+</sup>, 327, 285, 267

NMR (270 MHz, DMSO  $d_6$ ): 1.39 (s, 6H); 2.58 (dd, 13Hz, 9Hz, 2H), 3.43 (dd, 13Hz, 3Hz, 2H); 3.68 (m, 2H); 3.83 (m, 2H), 5.05 (d, 6Hz, 2H); 7.14-7.32 (m, 10H)

Synthesis analogous to example 2 from example 11

MS (FAB, LiI): 761 (M + Li)<sup>+</sup>, 755 (M + H)<sup>+</sup>, 737

### Examples 3-5

3) N,N'-bis-(tert.-butoxycarbonyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

- 4) N,N-bis-(tert.-butoxycarbonyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol
- 5) N,N-bis-(tert.-butoxycarbonyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4S-diol

17 g tert.-butoxycarbonyl-L-phenylalaninal were dissolved in 500 ml THF and cooled under argon to 0°C. Over about 20 min 1 l of 0.1 molar  $\text{SmI}_2$  solution in THF were added and the solution was stirred for 30 min at RT. The solution was acidified to pH 1-2 with 0.1 N aqueous HCl. The solution was diluted with EA, the organic phase was separated and extracted with 0.1 N HCl, twice with  $\text{Na}_2\text{S}_2\text{O}_3$  solution and twice with water. After drying over  $\text{MgSO}_4$  the solution was concentrated and chromatographed over silica gel (EA/petroleum ether 1/2).

The fraction containing the 3R,4R isomer was recrystallized from ethanol/water.

Through crystallization from dichloromethane/isopropyl ether/heptane it was possible to derive the 3S,4S isomer from the fraction containing the 3S,4S and the 3R,4S isomer. To obtain the 3R,4S isomer the mother liquor was chromatographed on RP18 silica gel (acetonitrile/water 4/6).

**Yields:** 1.61 g 3R,4R isomer

1.00 g 3S,4S isomer

0.71 g 3R,4S isomer

Rf values: silica gel, EA/hexane 1/2

0.18 3R,4R isomer

0.41 3S,4S isomer

0.39 3R,4S isomer

<sup>1</sup> H-NMR (270 Mhz, DMSO <D <sub>6</sub> >):			
	3R,4R isomer	3S,4S isomer	3R,4S isomer
N-H	6.16; (d; 2H)	6.60 (d, 2H)	6.31 (d, 1H) 6.28 (d, 1H)
O-H	4.43 (m, 2H)	4.57 (d, 7Hz, 2H)	4.62 (s, 4Hz, 1H) 4.94 (d, 6Hz, 1H)
H <sup>3</sup> , H <sup>4</sup>	4.12 (m, 2H)	3.71 (m, 2H)	3.91-4.12 (m, 2H)
H <sup>2</sup> , H <sup>5</sup>	3.24 (m, 2H)	3.42 (m, 2H)	3.27-3.46 (m, 2H)
CH <sub>2</sub>	2.54-2.80 (m, 2H)	3.04 (dd, 14Hz, 4Hz, 1H) 2.63 (dd, 14Hz, 9Hz, 1H)	2.62-2.83 (m, 2H)
C(CH <sub>3</sub> ) <sub>3</sub>	1.30 (s, 18H)	1.30 (s, 18H)	1.32 (s, 9H) 1.24 (s, 9H)
Ar-H	7.08-7.27 (m, 10H)	7.11-7.29 (m, 10H)	7.08-7.32 (m, 10H)

### Example 3.1

140 mg 2S,5S-diamino-1,6-diphenyl-3,4-O-isopropylidene-hexane-3R<4R-diol were dissolved in a mixture of 5 ml 1N HCl in methanol and 5 ml 5N HCl in dioxane and stirred for 4 h at RT. The volatile components were removed i. vac. The residue was dried in a high vacuum and the 2S,5S-diamino-1,6-

diphenyl-hexane-3R,4R-diol-dihydrochloride (MS (FAB): 301 (M + H)<sup>+</sup> of the free base) obtained was used directly in the next reaction.

45 mg 2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol-dihydrochloride were dissolved in 5 ml dry dichloromethane and together with 40  $\mu$ l triethylamine and 75 mg pyrocarboxylic-di-tert.-butyl ester stirred for 3 h at RT. The solution was diluted with dichloromethane and extracted with  $\text{KHSO}_4$ ,  $\text{NaHCO}_3$  and  $\text{NaCl}$  solutions. After drying over anhydrous  $\text{Na}_2\text{SO}_4$  the solution was concentrated and purified over silica gel (acetonitrile/DCM 1/8).

**Yield:** 23 mg

MS (FAB) 501 (M + H)<sup>+</sup>, 401, 345, 327, 301

The compound was identical to the most polar isomer from examples 3-5.

### Example 6

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

38 mg N,N'-bis-(tert.-butoxycarbonyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol were treated for 30 min with 5N HCl in dioxane. The volatile components were removed i. vac., and the residue was dried. The N,N'-bis-(L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol-dihydrochloride thus obtained was dissolved with 40 mg tert.-butoxycarbonyl-phenylalanine, 22 mg HOBt and 51 mg TBTU in 1 ml dry DMF. 60  $\mu$ l ethyldiisopropylamine were added and the solution was stirred for 15 min at RT. The DMF was spun off, the residue was taken up in EA and extracted with KHSO<sub>4</sub>, NaHCO<sub>3</sub> solutions and water. After drying over MgSO<sub>4</sub> the solution was concentrated, the substance crystallizing out. The precipitate was filtered off, washed with ether, and a yield of 30 mg was obtained.

MS (FAB): 1015 (M + Na)<sup>+</sup>, 993 (M + H)<sup>+</sup>, 893, 793

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.79 (m, 12H); 1.28 (s, 18H); 1.85 (m, 2H); 2.68-2.82 (m, 4H); 2.85-3.03 (m, 4H); 3.37 (m, 2H); 4.00-4.13 (m, 4H); 4.21 (m, 2H); 4.66 (d, 7Hz, 2H); 7.03 (d, 7Hz, 2H); 7.05-7.34 (m, 20H); 7.62 (d, 7Hz, 2H); 7.68 (d, 8Hz, 2H)

### Example 7

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4S-diol

Synthesis analogous to example 6 from N,N'-bis-(tert.-butoxycarbonyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4S-diol

MS (FAB): 1015 (M + Na)<sup>+</sup>, 993 (M + H)<sup>+</sup>, 893, 793

NMR (270 MHz, DMSO  $\text{-d}_6$ ): 0.68-0.85 (m, 12H); 1.28 (s, 9H); 1.30 (s, 9H); 1.75-2.03 (m, 2H); approx. 2.5-3.30 (m, 8H); approx. 3.3-3.51 (m, 2H); 4.05-4.30 (m, 5H); 4.43 (m, 1H); 4.74 (d, 4Hz, 1H); 5.32 (d, 7Hz, 1H); 6.93-7.35 (m, 22H); 7.61 (d, 8Hz, 1H); 7.67 (d, 7Hz, 1H); 7.85 (d, 8Hz, 1H); 7.92 (d, 7Hz, 1H)

### Example 8

N,N'-bis-(tert.-butoxycarbonyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

164 mg N,N'-bis-(tert.-butoxycarbonyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol were treated for 1.5 h at RT with 10 ml 5N HCl in dioxane. The volatile components were removed i. vac., the residue was dried. The 2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride thus obtained was dissolved in 15 ml dry DMF together with 178 mg tert.-butoxycarbonyl-L-valine

**Yield:** 59 mg

### Example 9

Synthesis analogous to example 8 from N,N'-bis-(tert.-butoxycarbonyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4S-diol

### Example 10

Synthesis analogous to example 2 from example 11

### Example 11

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**Yield:** 31 mg.

NMR (270 MHz, DMSO  $d_6$ ): 0.69 (d, 7Hz, 6H); 0.76 (d, 7Hz, 6H); 1.10 (s, 18H); 1.86 (m, 2H); 2.63-2.87 (m, 6H); 3.08 (m, 2H); c. 3.25-3.44 (m, c. 2H); 3.52-3.63 (m, 2H); 4.08 (m, 2H); 7.32 (d, 8 Hz, 2H); 7.38-7.48 (m, 4H); 7.47-7.62 (m, 4H); 7.81 (m, 2H); 7.92 (m, 2H); 8.12-8.25 (m, 4H)

**N,N'-bis-(L-seryl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride**

MS (FAB, LiI): 973 (M + Li)<sup>+</sup>, 967 (M + H)<sup>+</sup>

N,N'-bis-(tert.-butoxycarbonyl-L-(O-tert.-butyl-seryl)-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

81



N,N'-bis-(L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

MS (FAB): 793 (M + H)<sup>+</sup>, 775.

**N,N'-bis-(L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4S-diol dihydrochloride**

MS (FAB): 793 (M + H)<sup>+</sup>, 775

**N,N'-bis-(L-seryl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride**

MS (FAB): 967 (M + H)<sup>+</sup>

**N,N'-bis-(L-seryl-L-phenylalanyl-L-valyl-2S,5S-diamino-1,6-diphenyl-hexane-3R,4S-diol dihydrochloride**

MS (FAB): 967 (M + H)<sup>+</sup>

### Example 21

**Bis-(N-(1-phenylalanyl-L-valyl)-2S-amino-3-phenylpropyl)-amine-trihydrochloride**

Synthesis analogous to example 22

MS (FAB): 776 (M + H)<sup>+</sup>

### Example 22

**Bis-(N-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2S-amino-3-phenylpropyl)  
amine**

Synthesis analogous to example 6 from example 23

MS (FAB, LiI): 982 (M + Li)<sup>+</sup>, 976 (M + H)<sup>+</sup>

NMR (270 MHz, DMSO  $d_6$ ): 0.81 (m, 12H); 1.29 (s, 18H); 1.89 (m, 2H);  
c. 2.45-2.98 (m, c. 12H); 3.97 (m, 2H); 4.05-4.25 (m, 4H); 7.03 (d, 9Hz, 2H);  
7.10-7.31 (m, 20H); 7.65 (d, 8Hz, 2H); 7.84 (d, 8Hz, 2H)

### Example 23

**Bis-(N-(L-valyl)-2S-amino-3-phenylpropyl-amine trihydrochloride**

Synthesis analogous to example 16 from example 24

**MS (FAB):** 482 ( $M + H$ )<sup>+</sup>

### Example 24

**Bis-(N-(tert.-butoxycarbonyl-L-valyl)-2S-amino-3-phenylpropyl) amine**

Synthesis analogous to example 16 from example 25.

MS (FAB): 682 (M + H)<sup>+</sup>

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.73 (d, 6Hz, 6H); 0.77 (d, 6Hz, 6H); 1.38 (s, 18H); 1.65 (s, 18H); 1.82 (m, 2H); 2.42-c. 2.53 (m, c. 4H); 2.64 (dd, 14Hz,

8Hz, 2H); 2.84 (dd, 14Hz, 6Hz, 2H); 3.68 (m, 2H); 3.93 (m, 2H); 6.50 (d, 9Hz, 2H); 7.12-7.28 (m, 10H); 7.62 (d, 8Hz, 2H)

### Example 25

**Bis-(N-tert.-butoxycarbonyl-2S-amino-3-phenylpropyl)-amine hydrochloride**

9.6 g tert.-butoxycarbonyl-L-phenylalaninal together with 30.5 g  $\text{NH}_4\text{OAc}$  and 1.7 g  $\text{NaBH}_3\text{CN}$  were dissolved in 300 ml methanol and stirred for 6 h at RT. The solution was acidified with HCl to pH < 2. The product precipitates. It was digested with diethyl ether and water, dried in a high vacuum, and a yield of 3.1 g was obtained.

MS (FAB): 484 (M + H)<sup>+</sup>, 428, 372.

NMR (270 MHz; DMSO  $d_6$ ): 1.33 (s, 18H); 2.55-2.90 (m; 8H), 3.82 (m; 2H), 6.75 (m; 2H), 7.12-7.325 (m; 10H).

### Example 26

**N,N'-bis-(5S-amino-4S-hydroxy-7-methyl-octanoyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride**

Synthesis analogous to example 16.

MS (FAB): 643 (M + H)<sup>+</sup>, 625.

NMR (270 MHz; DMSO  $\text{d}_6$ ): 0.92 (m; 12H), 1.43 (m; 4H), 1.60 (m; 4H), 1.74 (m; 2H), 2.15 (m, 2H), 2.26 (m; 2H), 2.72 (dd, 14Hz, 11Hz, 2H), 2.93 (m; 2H), 3.12 (dm; 2H), 3.44 (m; 4H), 4.03 (m; 2H), c. 4.85 (m; c. 4H), 7.13–7.38 (m; 20H), 7.82 (m; 6H), 8.13 (d, 9Hz; 2H).

N,N'-bis-(N-tert.-butoxycarbonyl)-5S-amino-7-methyl-4S-(tert.-butyl-dimethylsilyl)oxy-octanoyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

**Yield:** 129 mg

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.02 (s; 6H), 0.08 (s; 6H), 0.77-0.93 (m; 30H), c. 1.1-1.4 (m; c. 6H), 1.45-1.63 (m; 4H), 1.91 (m; 2H), 2.02-2.16 (m; 2H), 2.67 (dd, 11Hz, 14Hz; 2H), 3.36 (m; 2H), 3.42-3.56 (m; 4H), 3.95 (m; 2H), 4.81 (d, 6Hz; 2H), 6.44 (d, 8Hz; 2H), 7.08-7.30 (m; 10H), 7.79 (d, 9Hz; 1H).

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-3S,6S-diamino-1,8-di-(4-pyridyl)-octane-4R,5R-diol

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.85 (d, 6Hz, 12H); 1.20 (s, 18H); 1.66 (m, 2H); 1.78 (m, 2H); 2.00 (m, 2H); c. 2.48 (m, 4H); 2.98 (m, 2H); c. 3.31 (m, 2H); 4.08 (m, 2H); 4.19 (m, 2H); 4.30 (m, 2H); 4.68 (m, 2H); 7.01 (d, 8Hz, 2H); 7.10–7.30 (m, 14H); 7.62 (d, 8Hz, 2H); 7.74 (d, 8Hz, 2H); 8.43 (d, 4.8 Hz, 4H)

MS (FAB): 1023 (M + H)<sup>+</sup>, 923, 823.

**3S,6S-diamino-1,8-di-(4-pyridyl)octane-4R,5R-diol tetrahydro-chloride**

Synthesis analogous to examples 2, 2b, 2c and 2e proceeding from 1,2R-5R,6-diepoxy-3,4-O-isopropylidene-3R,4R-diol and 4-picolyllithium.

NMR (270 MHz, DMSO  $d_6$ ): 1.87-2.20 (m, 4H); 3.10 (m, 4H); 3.29 (m, 2H); 3.84 (d, 6Hz, 2H); c. 3.3-4.5 (br, c. 4H); 8.07 (d, 7Hz, 4H); 8.18 (m, 6H); 8.88 (d, 7Hz, 4H).

MS (FAB): 331 (M + H)<sup>+</sup>

N,N'-bis-(2S-<2S-amino-3-phenyl-propyl>-amino-3-methyl-butanoyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol tetrahydrochloride

Synthesis analogous to example 16.

MS (FAB): 765 (M + H)<sup>+</sup>

N,N'-bis-(2S-<2S-tert.-butoxycarbonylamino-3-phenyl-propyl>-amino-3-methyl-  
butanoyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

**Yield:** 33 mg

NMR (270 MHz; DMSO  $\text{d}_6$ ): 0.74 (d, 7Hz, 6H); 0.78 (d, 6Hz, 6H); 1.33 (s, 18H); 1.63 (m, 2H); 1.94-2.16 (m, 4H); c. 2.5 (m, c. 4H); 2.64 (m, 2H); 2.81 (dd, 14Hz, 5Hz, 2H); 3.13 (dm, 14Hz, 2H); 3.42 (m, 2H); 3.56 (m, 2H); 4.10 (m, 2H); 4.90 (m, 2H); 6.58 (d, 9Hz, 2H); 7.05-7.30 (m, 20H); 7.85 (d, 8Hz, 2H)

**N,N'-bis-(L-phenylalanyl-L-valyl)-2R,5R-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride**

MS (FAB): 793 (M + H)<sup>+</sup>

**N,N'-bis-(L-phenylalanyl-L-valyl)-2R,5R-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride**

Synthesis analogous to example 16.

MS (FAB): 793 (M + H)<sup>+</sup>

**N,N'-bis-(L-phenylalanyl-L-valyl)-2R,5R-diamino-1,6-diphenyl-hexane-3R,4S-diol dihydrochloride**

Synthesis analogous to example 16.

MS (FAB): 793 (M + H)<sup>+</sup>

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2R,5R-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 993 (M + H)<sup>+</sup>, 893, 793

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.48 (d, 7Hz, 6H); 0.54 (d, 6Hz, 6H); 1.25 (s, 18H); 1.70 (m, 2H); 2.60 (t, 13Hz, 2H); 2.74 (dd, 14Hz, 11Hz, 2H); 2.96 (dd, 13Hz, 4Hz, 2H); 3.13 (dm, 14Hz, 2H); 3.39 (m, 2H); 4.02-4.25 (m, 6H); 4.88 (d, 4Hz, 2H); 7.02 (d, 9Hz, 2H), 7.07-7.33 (m, 20H); 7.60 (d, 9Hz, 2H); 8.24 (d, 9Hz, 2H).

## (3)

**N,N-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2R,5R-diamino-1,6-diphenyl-hexane-3S,4S-diol**

Synthesis analogous to example 6.

MS (FAB): 993 (M + H)<sup>+</sup>, 893, 793.

### Example 35

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2R,5R-diamino-1,6-diphenyl-hexane-3R,4S-diol

Synthesis analogous to example 6.

MS (FAB): 993 (M + H)<sup>+</sup>, 893, 793.

### Examples 36-38

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Synthesis analogous to examples 3-5 from tert.-butoxycarbonyl-D-phenylalaninal. The MS and NMR data correspond to those of their enantiomorphs from examples 3-5.

### Example 39

N,N'-bis-(L-(1-naphthyl)alanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

MS (FAB, LiI): 899 (M + Li)<sup>+</sup>, 893 (M + H)<sup>+</sup>, 875.

**N,N'-bis-(tert.-butoxycarbonyl-L-(1-naphthyl)alanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol**

MS (FAB): 1093 (M + H)<sup>+</sup>, 993.

NMR (270 MHz, DMSO  $\text{-d}_6$ ): 0.76 (m, 12H); 1.23 (s, 18H); 1.89 (m, 2H); 2.60-2.87 (m, 4H); 3.12 (dd, 14Hz, 10Hz, 2H); c. 3.33 (m, 2H); 3.52 (dm, 4Hz, 2H); 4.16-4.35 (m, 4H); 4.44 (m, 2H); 4.70 (s, 2H); 7.00-7.27 (m, 12H); 7.37-7.44 (m, 4H); 7.46-7.68 (m, 8H); 7.79 (m, 2H); 7.92 (d, 8Hz, 2H); 8.13 (d, 8Hz, 2H).

N,N'-bis-[(2-(2-hydroxyethyl-sulfonylmethyl)-3-phenylpropionyl)-L-valyl]-  
2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 13.

MS (FAB): 1007 (M + H)<sup>+</sup>

N,N'-bis-[L-phenylalanyl-L-valyl]-2S,5S-diamino-1,6-dicyclohexyl-hexane-3R,4R-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 805 (M + H)<sup>+</sup>, 787.

N,N'-bis-[L-phenylalanyl-L-valyl]-2S,5S-diamino-1,6-dicyclohexyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 805 (M + H)<sup>+</sup>, 787.

### Example 44

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-dicyclohexyl-hexane -3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 1005 (M+H)<sup>+</sup>, 987, 905, 805.

### Example 45

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-dicyclohexyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 1005 (M+H)<sup>+</sup>, 987, 905, 805.

NMR (270 MHz, DMSO  $d_6$ ): 0.86 (m, 12H); 0.99-1.67 (m, c. 24H); 1.28 (s, 18H); 1.74 (m, 2H); 1.98 (m, 2H); 2.75 (dd, 14Hz, 11Hz, 2H); 2.96 (dd, 14Hz, 4Hz, 2H); 3.23 (m, 2H); 3.89 (m, 2H); 4.13-4.25 (m, 2H); 4.42 (d, 5Hz, 2H); 7.02 (d, 8Hz, 2H); 7.13-7.32 (m, 20H); 7.69-7.81 (m, 4H).

### Example 46

N,N'-bis-(tert.-butoxycarbonyl)-2S,5S-diamino-1,6-dicyclohexyl-hexane-3S,4S-diol



N,N'-bis-(4Z-aminocyclohexanecarbonyl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-3S,5S-diol dihydrochloride

Synthesis analogous to example 16 or 6.

MS (FAB): 1043 (M+H)<sup>+</sup>, 1025.

### Example 50

N,N'-bis-(4Z-N-tert.-butoxycarbonylamino)-cyclohexanecarbonyl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-3S,5S-diol dihydrochloride

Synthesis analogous to example 6.

MS (FAB): 1243 (M+H)<sup>+</sup>, 1143, 1043.

### Example 51

N,N'-bis- $\alpha$ -(2S-(1,2-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl)-L-valyl- $\alpha$ -(2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol)

Synthesis analogous to example 13.

MS (FAB): 1131 (M+H)<sup>+</sup>, 716.

NMR (270 MHz, DMSO  $d_6$ ): 0.77 (d, 7Hz, 6H); 0.80 (d, 7Hz, 6H); 1.12 (s, 18H); 1.87 (m, 2H); 2.75 (m, 2H); 2.83 (m, 2H); 2.92-3.03 (m, 2H); 3.10-3.22 (m, 2H); c. 3.27-3.49 (m, 6H); 3.54-3.67 (m, 2H); 4.02-4.15 (m, 4H); 4.66 (d, 6Hz, 2H); 7.01-7.09 (m, 2H); 7.10-7.25 (m, 8H); 7.28-7.43 (m, 4H); 7.48-7.68 (m, 6H); 7.79 (d, 8Hz, 2H); 7.88-7.95 (m, 2H); 8.15-8.25 (m, 4H).

### Example 52

N,N'-bis-(2S-(1,1-dimethylethyl-sulfonylmethyl)-3-phenylpropionyl)-L-valyl-  
2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol



**N,N'-bis-( $\alpha$ -L-phenylalanyl-L-valyl)-4S,7S-diamino-2,9-dimethyl-decane-5,6-diol dihydrochloride**

MS (FAB): 725 (M+H)<sup>+</sup>

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-4S,7S-diamino-2,9-dimethyl-decane-5,6-diol dihydrochloride

MS (FAB): 925 (M+H)<sup>+</sup>, 826, 725

NMR (270 MHz, DMSO  $d_6$ ): 0.75-0.95 (m, 24H); 1.29 (s, 18H); 1.35-1.45 (m, 4H); 1.56 (m, 2H); 1.99 (m, 2H); 2.74 (dd, 10Hz, 13H, 2H); 2.95 (dd, 4Hz, 13Hz, 2H); 3.23 (m, 2H); 3.88 (m, 2H); 4.13-4.28 (m, 4H); 4.45 (d, 5Hz, 2H); 7.02 (8d, 8Hz, 2H); 7.13-7.33 (m, 10H); 7.76 (d, 8Hz, 2H), 7.80 (d, 8Hz, 2H).

N,N'-bis-(2S-(1,1-dimethylethyl-sulfonylmethyl)-3-phenylpropionyl)-L-valyl-4S,7S-diamino-2,9-dimethyl-decane-3,4-diol

MS (FAB): 985 (M+Na)<sup>+</sup>, 963 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $d_6$ ): 0.78 (d, 7Hz, 6H); 0.80-0.93 (m, 18H); 1.15 (s, 18H); 1.20-1.68 (m, 6H); 1.98 (m, 2H); 2.58 (dd, 10Hz, 14Hz, 2H); 2.73 (dd, 14Hz, 3Hz, 2H); 2.98 (dd, 14Hz, 4Hz, 2H); 3.23 (m, 2H); c. 3.33 (m, 2H); 3.47-3.61 (m, 2H); 3.85 (m, 2H); 4.14 (m, 2H); 4.44 (d, 5Hz, 2H); 7.15-7.33 (m, 10H); 7.69 (d, 9Hz, 2H); 8.22 (d, 9Hz, 2H).

### Example 58

N,N'-bis- $\langle$ (2-pyridyl)-acetyl-L-valyl $\rangle$ -2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

74 mg 2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydro-chloride and 68 mg 2-pyridyl acetyl hydrochloride were dissolved in 2 ml DMF, and 53 mg HOBt, 125 mg TBTU and 0.221 ml diisopropyl-ethylamine were added. The solution was stirred for 2 h at RT and worked up as usual. After chromatography on silica gel (DCM/MeOH 95/5 to 90/10) 68 mg of product were obtained.

MS (FAB): 759 (M+Na)<sup>+</sup>, 737 (M+H)

NMR (270 MHz, DMSO  $\langle$ D6 $\rangle$ ): 0.70 (2d, 12H); 1.88 (m, 2H); 2.62 (dd, 14Hz, 5Hz, 2H); 2.77 (dd, 14Hz, 10Hz, 2H); 3.72 (m, 4H); 4.13 (dd, 6Hz, 9Hz, 2H); 4.46 (m, 2H); 7.05-7.23 (m, 10H); 7.28-7.40 (m, 4H); 7.48 (d, 9Hz, 2H); 7.82 (dt, 8Hz, 2H); 7.97 (d, 9Hz, 2H); 8.54 (m, 2H).

### Example 59

N,N'-bis- $\langle$ (4-pyridyl-thio)-acetyl-L-valyl $\rangle$ -2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

74 mg 2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride and 66 mg 4-pyridylmercaptoacetic acid were dissolved in 2 mg DMF, and 53 mg HOBt, 125 mg TBTU and 0.177 ml diisopropylamine were added. The solution was stirred for 2 h at RT, the solvent was removed i. vac. and the residue was stirred for 30 min between EA and NaHCO<sub>3</sub> solution. The insoluble part was filtered off and washed with EA and water. The raw product was dissolved in warm DMF, the solution filtered and stirred in EA. The precipitate was suctioned off and dried. Yield: 76 mg.

MS (FAB): 801 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.68 (2d, 12H); 1.84 (m, 2H); 2.62 (dd, 14Hz, 5Hz, 2H); 2.78 (dd, 14Hz, 9Hz, 2H); 3.28 (m, 2H); 3.73 (d, 15Hz, 2H); 3.90 (d, 15Hz, 2H); 4.17 (dd, 6Hz, 9Hz, 2H); 4.43 (m, 2H); 4.70 (m, 2H); 7.05-7.20 (m, 10H); 7.30 (m, 4H); 7.58 (d, 9Hz, 2H); 8.03 (d, 9Hz, 2H); 8.34 (m, 4H).

#### Example 60

N,N'-bis-<L-phenylalanyl-D-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 793 (M+H)<sup>+</sup>

#### Example 61

N,N'-bis-<D-phenylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 793 (M+H)<sup>+</sup>

#### Example 62

N,N'-bis-<tert.-butoxycarbonyl-L-phenylalanyl-D-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 993 (M+H)<sup>+</sup>, 893, 793.

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.42 (d, 7Hz, 6H); 0.47 (d, 7Hz, 6H); 1.26 (s, 18H); 2.58 (m, 2H); 2.73 (m, 2H); 2.98 (dd, 13Hz, 5Hz, 2H); 3.16 (m, 2H);

3.40 (m, 2H); 4.00-4.32 (m, 6H); 4.85 (d, 5Hz, 2H); 6.86 (d, 9Hz, 2H); 7.07-7.30 (m, 20H); 7.74 (d, 9Hz, 2H); 8.19 (d, 9Hz, 2H).

### Example 63

N,N'-bis-<tert.-butoxycarbonyl-D-phenylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 1015 (M+Na)<sup>+</sup>, 993 (M+H)<sup>+</sup>, 893, 793

NMR (270 MHz, DMSO  $d_6$ ): 0.72 (d, 7Hz, 12H); 1.30 (s, 18H); 1.84 (s, 2H); 2.65-2.82 (m, 4H); 2.88-3.02 (m, 4H); 3.37 (m, 2H); 4.00-4.13 (m, 4H); 4.28 (m, 2H); 4.63 (d, 7Hz, 2H); 6.96 (d, 8Hz, 2H); 7.05-7.35 (m, 20H); 7.59 (d, 8Hz, 2H); 7.82 (d, 9Hz, 2H).

### Example 64

N,N'-bis-<L-phenylalanyl-glycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16

MS (FAB): 709 (M+H)<sup>+</sup>.

### Example 65

N,N'-bis-<L-phenylalanyl-L-isoleucyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 821 (M+H)<sup>+</sup>

### Example 66

N,N'-bis-<L-leucyl-glycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 20.

MS (FAB): 641 (M+H)<sup>+</sup>

### Example 67

N,N'-bis-<tert.-butoxycarbonyl-L-phenylalanyl-glycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S diol

Synthesis analogous to example 6.

MS (FAB): 931 (M+Na)<sup>+</sup>, 909 (M+H)<sup>+</sup>, 809, 709

NMR (270 MHz, DMSO <D<sub>6</sub>>): 1.38 (s, 18H); 2.58-2.78 (m, 4H); 2.92-3.09 (m, 4H); 3.43-3.62 (m, 4H); 3.78 (dd, 16Hz, 5Hz, 2H); 4.05 (m, 2H); 4.19 (m, 2H); 4.83 (d, 5Hz, 2H); 6.92 (d, 9Hz, 2H); 7.10-7.29 (m, 10H); 7.90 (d, 9Hz, 2H); 8.01 (m, 2H).

### Example 68

N,N'-bis-<tert.-butoxycarbonyl-L-phenylalanyl-L-isoleucyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 1021 (M+H)<sup>+</sup>, 921, 821

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.70-0.85 (m, 12H); 1.03 (m, 2H); 1.29 (s, 18H); 1.37 (m, 2H); 1.65 (m, 2H); 2.68-2.80 (m, 4H); 2.84-3.04 (m, 4H); 3.39 (m, 2H); 4.00-4.13 (m, 4H); 4.20 (m, 2H); 4.64 (d, 7Hz, 2H); 7.02 (d, 9Hz, 2H); 7.05-7.33 (m, 20H); 7.62-7.73 (m, 4H).

### Example 69

N,N'-bis-<tert.-butoxycarbonyl-L-leucyl-glycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 863 (M+Na)<sup>+</sup>, 841 (M+H)<sup>+</sup>, 741, 641

NMR (270 MHz, DMSO  $d_6$ ): 0.83 (d, 6Hz, 6H); 0.87 (d, 6Hz, 6H); 1.38 (s, 18H); c. 1.42 (m, 4H); 1.60 (m, 2H); 2.62 (dd, 14Hz, 10Hz, 2H); 3.03 (dm, 14Hz, 2H); 3.44 (m, 2H); 3.52 (dd, 16Hz, 5Hz, 2H); 3.72 (dd, 16Hz, 5Hz, 2H); 3.90-4.08 (m, 4H); 4.79 (d, 5Hz, 2H); 6.93 (d, 9Hz, 2H); 7.10-7.28 (m, 10H); 7.78-7.90 (m, 4H).

### Example 70

N,N'-bis-<L-phenylalanyl-L-seryl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 769 (M+H)<sup>+</sup>

### Example 71

N,N'-bis-<5S-amino-4S-hydroxy-7-methyl-2R-propyl-octanoyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

56 mg 2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride and 134 mg N-tert.-butoxycarbonyl-5S-amino-7-methyl-2R-propyl-4S-(tert.-butyl-dimethylsilyl-oxy)-octanoic acid were dissolved in 3 ml DMF, and 43 mg HOBt, 101 mg TBTU and 155 mg diisopropylethylamine were added. The solution was stirred for 4 h at RT, the solvent was removed i. vac. and the residue was divided between DCM and water. The organic phase was extracted with KHSO<sub>4</sub>

solution,  $\text{NaHCO}_3$  solution and water. After drying over anhydrous sodium sulfate the solution was concentrated and the residue was chromatographed on silica gel (cyclohexane/EA 3/1). The yield obtained was 157 mg N,N'-bis-<N-tert.-butoxycarbonyl-5S-amino-7-methyl-2R-propyl-4S-(tert.-butyldimethylsilyl-oxy)-actanoyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride. Treatment with HCl in dioxane analogous to example 16 yielded the product.

The coupling component N-tert.-butoxycarbonyl-5S-amino-7-methyl-2R-propyl-4S-(tert.-butyldimethylsilyl-oxy)-octanoic acid was prepared analogous to the description in example 27.

For this, the initial material (5S)-5-<(1S)-1-(N-Boc-amino)-3-methylbutyl>dihydrofuran-2(3H)-on was additionally alkylated with allyl bromide and then hydrogenated (analogous to the preparation of compound 11 in Fray, et al.).

MS (FAB): 727 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.80-0.88 (m, 18H); 1.08-1.74 (m, 18H); c. 2.55 (m, 2H); 2.72-2.88 (m, 4H); 3.02-3.18 (m, 4H); 3.48 (d, 7Hz, 2H); 3.99 (m, 2H); 7.10-7.19 (m, 2H); 7.20-7.32 (m, 10H); 7.74 (m, 6H); 8.16 (d, 9Hz, 2H).

### Example 72

N,N'-bis-<L-phenylalanyl-L-cyclohexylglycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 873 (M+H)<sup>+</sup>

### Example 73

N,N'-bis-<tert.-butoxycarbonyl-L-phenylalanyl-L-cyclohexylglycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6

MS (FAB): 1073 (M+H)<sup>+</sup>, 973, 873

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.82-1.66 (m, c. 22H); 1.29 (s, 18H); 2.56-2.97 (m, 8H); c. 3.30 (m, 2H); 4.08-4.22 (m, 4H); 4.50 (m, 2H); 4.63 (m, 2H); 7.02 (d, 9Hz, 2H); 7.04-7.32 (m, 20H); 7.47 (d, 9Hz, 2H); 7.56 (d, 9Hz, 2H).

### Example 74

N,N'-bis-<L-methionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 761 (M+H)<sup>+</sup>

### Example 75

N,N'-bis-<tert-butoxycarbonyl-L-methionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 961 (M+H)<sup>+</sup>, 861, 761

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.75 (d, 6Hz, 12H); 1.38 (s, 18H); 1.70-1.90 (m, 6H); 2.02 (s, 6H); c. 2.37-2.5 (m, 4H); c. 3.32 (m, 2H); 3.94-4.10 (m, 6H); 4.63 (d, 7Hz, 2H); 7.04-7.20 (m, 12H); 7.49-7.59 (m, 4H).

### Example 76

N,N'-bis-<(O-methyl-tyrosyl)-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 853 (M+H)<sup>+</sup>

### Example 77

N,N'-bis-<tert.-butoxycarbonyl-(O-methyl-tyrosyl)-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 16.

MS (FAB): 1053 (M+H)<sup>+</sup>, 953, 853

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.73-0.83 (m, 12H); 1.29 (s, 12H); 1.84 (m, 2H); 2.60-3.02 (m, 8H); 3.36 (m, 2H); 3.70 (s, 6H); 4.64 (d, 6Hz, 2H); 6.82 (d, 9Hz, 4H); 6.98 (d, 9Hz, 2H); 7.05-7.22 (m, 14H); 7.59 (d, 9Hz, 2H); 7.65 (d, 9Hz, 2H).

### Example 78

N,N'-bis-<L-tyrosyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 825 (M+H)<sup>+</sup>

### Example 79

N,N'-bis-<(N-tert.-butoxycarbonyl-O-tert.-butyl-L-tyrosyl)-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 1137 (M+H)<sup>+</sup>, 1037, 937

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.72-0.85 (m, 12H); 1.25 (s, 18H); 1.28 (s, 18H); 1.85 (m, 2H); 2.62-2.82 (m, 4H); 2.84-3.01 (m, 4H); 3.36 (m, 2H); 3.98-4.12 (m, 4H); 4.19 (m, 2H); 4.64 (d, 7Hz, 2H); 6.85 (d, 8Hz, 4H); 7.02 (d, 9Hz, 2H); 7.05-7.21 (m, 18H); 7.60 (d, 8Hz, 2H); 7.66 (d, 9Hz, 2H).

#### Example 80

N,N'-bis-<N<sup>6</sup>-benzyloxycarbonyl-N<sup>2</sup>-(tert.-butoxycarbonyl-L-lysyl)-L-valyl>2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB/LiI): 1229 (M+H)<sup>+</sup>

#### Example 81

N,N'-bis-<N<sup>6</sup>-benzyloxycarbonyl-N<sup>2</sup>-(tert.-butoxycarbonyl-L-phenylalanyl)-L-lysyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 1319 (M+H)<sup>+</sup>, 1219, 1185

NMR (270 MHz, DMSO <D<sub>6</sub>>): 1.08-1.47 (m, 30H); 2.60-2.82 (m, 6H); 2.87-3.00 (m, 6H); 3.23 (m, 2H); 4.08-4.23 (m, 4H); 4.36 (m, 2H); 4.69 (m, 2H); 4.99 (s, 4H); 6.94 (d, 9Hz, 2H); 7.04-7.40 (m, 32H); 7.46 (d, 8Hz, 2H); 7.69 (d, 9Hz, 2H).

#### Example 82

N,N'-bis-<L-glutamyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB/LiI): 763 (M+Li)<sup>+</sup>, 757 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $\text{<D}_6\text{>}$ ): 0.81 (d, 6Hz, 6H); 0.85 (d, 6Hz, 6H); 0.78-1.98 (m, 6H); 2.20-2.38 (m, 4H); 2.76 (m, 2H); 2.97 (m, 2H); c. 3.35 (m, c. 2H); 3.89 (m, 2H); 4.01-4.14 (m, 4H); 4.68 (d, 7Hz, 2H); 7.06-7.21 (m, 10H); 7.68 (d, 8Hz, 2H); 8.22 (m, 6H); 8.46 (d, 9Hz, 2H).

### Example 83

N,N'-bis-<tert.-butoxycarbonyl-L-glutamyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis from example 84 by catalytic hydrogenation on Pd/carbon in glacial acetic acid/water 9/1.

MS (FAB): 979 (M+Na)<sup>+</sup>, 958 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $\text{<D}_6\text{>}$ ): 0.70-0.82 (m, 12H); 1.38 (s, 18H); 1.62-1.93 (m, 6H); 2.17-2.29 (m, 4H); 2.74 (m, 2H); 2.95 (dm, 13Hz, 2H); c. 3.35 (m, 2H); 3.90-4.09 (m, 6H); 4.12 (m, 2H); 7.00-7.20 (m, 12H); 7.48-7.62 (m, 4H).

### Example 84

N,N'-bis-<(N-tert.-butoxycarbonyl-O-benzyl-L-glutamyl)-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 1159 (M+Na), >, 11

NMR (270 MHz, DMSO  $\text{<D}_6\text{>}$ ): 0.75 (d, 6Hz, 18H); 1.37 (s, 18H); 1.70-1.98 (m, 6H); 2.33-2.45 (m, 2H); 2.76 (m, 2H); 2.93 (m, 2H); c. 3.3 (m, 2H); 3.94-4.08 (m, 6H); 4.60 (s, 7Hz, 2H); 5.08 (s, 4H); 7.03-7.17 (m, 12H); 7.30-7.48 (m, 10H); 7.50 (d, 8Hz, 2H); 7.58 (d, 9Hz, 2H).

#### Example 85

N,N'-bis-<glycyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 635 (M+Na)<sup>+</sup>, 613 (M+H)<sup>+</sup>

#### Example 86

N,N'-bis-<tert.-butoxycarbonyl-glycyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 835 (M+Na)<sup>+</sup>, 813 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.70 (d, 7Hz, 12H); 1.38 (s, 18H); 1.84 (m, 2H); 2.62 (dd, 14Hz, 4Hz, 2H); 2.87 (dd, 14Hz, 10Hz, 2H); 3.26 (m, 2H); 3.52 (d, 6Hz, 4H); 4.13 (m, 2H); 4.42 (m, 2H); 4.69 (m, 2H); 7.03 (m, 2H); 7.08-7.21 (m, 10H); 7.38 (d, 9Hz, 2H); 7.50 (d, 9Hz, 2H).

#### Example 87

N,N'-bis-<L-leucyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 747 (M+Na)<sup>+</sup>, 725 (M+H)<sup>+</sup>

#### Example 88

N,N'-bis-<tert.-butoxycarbonyl-L-leucyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 6.

MS (FAB): 947 (M+Na)<sup>+</sup>, 925 (M+H)<sup>+</sup>, 825, 725

NMR (270 MHz, DMSO  $\langle D_6 \rangle$ ): 0.72-0.80 (m, 12H); 0.85 (d, 7Hz, 6H); 0.89 (d, 7Hz, 6H); 1.28-1.54 (m, 22H); 1.60 (m, 2H); 1.81 (m, 2H); 2.76 (dd, 13Hz, 9Hz, 2H); 2.93 (dd, 13Hz, 4Hz, 2H); c. 3.33 (m, 2H); 3.92-4.09 (m, 6H); 4.60 (d, 7Hz, 2H); 7.04 (d, 8Hz, 2H); 7.05-7.20 (m, 10H); 7.48 (d, 9Hz, 4H).

#### Example 89

N,N'-bis-<L-(S-dioxo)methionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 847 (M+Na)<sup>+</sup>, 825 (M+H)<sup>+</sup>

#### Example 90

N,N'-bis-<tert.-butoxycarb!nyl-L-(S-dioxo)methionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R-4R-diol

Synthesis analogous to example 6.

MS (FAB): 1074 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $\langle D_6 \rangle$ ): 0.65-0.78 (m, 12H); 1.39 (s, 18H); 1.74-2.07 (m, 6H); 2.63 (m, 2H); 2.78 (m, 2H); 3.07 (m, 4H); 3.26 (m, 2H); 3.98-4.17 (m, 4H); 4.44 (m, 2H); 4.67 (m, 2H); 7.07-7.23 (m, 12H); 7.49 (d, 9Hz, 2H); 7.53 (d, 9Hz, 2H).

#### Example 91

N,N'-bis-<(2S-(1,1-dimethylethyl-sulfonylmethyl)-3-phenylpropionyl)-L-tert.-butylglycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 13.

MS (FAB): 1081 (M+Na)<sup>+</sup>, 1059 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $d_6$ ): 0.83 (s, 18H); 1.12 (s, 18H); 2.39 (dd, 11Hz, 14Hz, 2H); 2.56-2.72 (m, 4H); 2.73-2.90 (m, 4H); c. 3.25-3.40 (m, c. 4H); 3.53 (dd, 10Hz, 2H); 4.20 (d, 9Hz, 2H); 4.54 (m, 2H); 4.62 (m, 2H); 6.98 (m, 2H); 7.07-7.36 (m, 18H); 7.47 (d, 9Hz, 2H); 7.98 (d, 9Hz, 2H).

### Example 92

N,N'-bis-((2S-(1,1-dimethylethyl-sulfonylmethyl)-3-phenylpropionyl)-L-neopentylglycyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 13.

MS (FAB): 1109 (M+Na)<sup>+</sup>, 1087 (M+H)<sup>+</sup>

NMR (270 MHz, CDCl<sub>3</sub>): 0.86 (s, 18H); 1.08 (dd, 8Hz, 14Hz, 2H); 1.35 (s, 18H); 1.58 (dd, 14Hz, 4Hz, 2H); 2.75-3.45 (m, c. 8H); 3.80 (m, 2H); 4.12 (m, 2H); 5.80 (d, 8Hz, 2H); 6.27 (d, 8Hz, 2H); 7.10-7.36 (m, c. 10H).

### Example 93

N,N'-bis-((2S-hydroxy-3-phenylpropionyl)-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Added to 0.065 mmol N,N'-bis-((L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol hydrochloride and 33 mg S-phenyl lactic acid in 4 ml DMF were 27 mg HOBt, 64 mg TBTU and then, slowly, 0.088 ml diisopropylethylamine. After 15 min at RT the DMF was removed in a vacuum, the residue was taken up in EA and extracted with KHSO<sub>4</sub> solution, NaHCO<sub>3</sub> solution and water. The organic phase was dried with MgSO<sub>4</sub> and concentrated, the residue was triturated with ether and suctioned off.

Yield: 43 mg.

MS (FAB): 795 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $<D_6>$ ): 0.63 (d, 7Hz, 6H); 0.67 (d, 7Hz, 6H); 1.82 (m, 2H); 2.64-2.79 (m, 4H); 2.91-3.04 (m, 4H); 3.38 (m, 2H); 3.97-4.17 (m, 6H); 4.72 (d, 6Hz, 2H); 5.77 (d, 6Hz, 2H); 7.08-7.29 (m, 20H); 7.38 (d, 9Hz, 2H); 7.85 (d, 8Hz, 2H).

#### Example 94

N,N'-bis- $<(2S\text{-hydroxy-4-phenylbutyryl})\text{-L-valyl}>$ -2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

Synthesis analogous to example 93

MS (FAB): 845 (N+Na)<sup>+</sup>, 823 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $<D_6>$ ): 0.73 (d, 5Hz, 6H); 0.76 (d, 5Hz, 6H); 1.76-2.00 (m, 6H); 2.55-2.78 (m, 6H); 2.98 (dm, 14Hz, 2H); 3.39 (m, 2H); 3.89 (m, 2H); 4.00-4.18 (m, 4H); 4.75 (d, 6Hz, 2H); 5.88 (d, 6Hz, 2H); 7.05-7.32 (m, 20H); 7.45 (d, 9Hz, 2H); 7.88 (d, 8Hz, 2H).

#### Example 95

N,N;-bis- $<(2\text{-(1-imidazolylmethyl)-3-phenyl-propionyl})\text{-L-valyl}>$ -2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol (from "diastereomer 1")

35.8 mg 2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-dioldihydro-chloride were dissolved with 90 mg 2-(1-imidazolyl-methyl)-3-phenyl-propionyl-L-valine ("diastereomer 1") in 2 ml DMF, and 32 mg HOBt, 77 mg TBTU and subsequently 0.163 ml diisopropylethylamine were added at RT. The solution was stirred for 3 h, the solvent was removed i. vac. and the residue was divided between EA and NaHCO<sub>3</sub> solution. The organic phase was washed with semi-concentrated NaCl solution, dried and concentrated. The residue was triturated with diethyl

MS (FAB): 923 (M+H)<sup>+</sup>

0.34 = diastereomer 1

0.18 = diastereomer 2

Saponification with NaOH in dioxane/water led to the coupling components for examples 95 and 96.

### Example 96

N,N'-bis-(2-(1-imidazolylmethyl)-3-phenyl-propionyl)-L-valyl>2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol (from "diastereomer 2")

For preparation see example 95.

MS (FAB): 923 (M+H)<sup>+</sup>

### Example 97

N,N'-bis-<3-(4-amino-1-piperidyl-sulfonyl)-2-benzylpropionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 16.

MS (FAB): 1115 (M+H)<sup>+</sup>

### Example 98

N,N'-bis-<2-benzyl-3-(4-tert.-butoxycarbonyl-amino-1-piperidyl-sulfonyl)-propionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol.

57 mg N,N'-bis-<L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride and 129 mg 2-benzyl-3-(4-tert.-butoxy-carbonyl-amino-1-piperidyl-sulfonyl)-propionic acid were dissolved in 1 ml DMF, and 41 mg HOBt, 96 mg TBTU and 135  $\mu$ l diisopropylethylamine were added. After 20 min the solvent was removed i. vac., the residue was taken up in DCM and extracted with KHSO<sub>4</sub> solution, KHCO<sub>3</sub> solution and water. After drying and concentrating, the viscous residue was dissolved in a little DCM/MeOH and precipitated with diethyl ether. Yield: 64 mg.

MS (FAB): 1337 (M+Na)<sup>+</sup>, 1315 (M+H)<sup>+</sup>, 1237, 1215, 1137, 1115

2-benzyl-3-(4-tert.-butoxycarbonyl-amino-1-piperidylsulfonyl)-propionic acid was synthesized analogous to example 13 according to: J. Med. Chem. 31 1839 (1988). The intermediate stage of the benzylacrylic ester was converted with thioacetic acid to 3-acetylthio-2-benzylpropionic benzyl ester. Subsequent oxidation with chlorine produced 2-benzyl-3-chlorosulfonyl-propionic benzyl ester was converted into the coupling component above by coupling with 4-tert.-butoxycarbonylamino-piperidine subsequent hydrogenation.

#### Example 99

N,N'-bis-<3-(4-amino-1-piperidyl-carbonyl)-2R-benzylpropionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 1043 (M+H)<sup>+</sup>

#### Example 100

N,N'-bis-<2R-benzyl-3-(4-tert.-butoxycarbonyl-amino-1-piperidyl-carbonyl)-propionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

57 mg N,N'-bis-<L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride and 129 mg 2R-benzyl-3-(4-tert.-butoxycarbonyl-amino-1-piperidyl-carbonyl)-propionic acid (synthesis by coupling of 4-tert.-butoxycarbonylamino-piperidine to 2-R-benzyl-3-carboxypropionic benzyl ester <see literature reference in example 102>) were dissolved in 1 ml DMF, and 41 mg HOBt, 96 mg TBTU and then, slowly, 0.135 ml diethylisopropylamine were added. After 20 min the solvent was removed i. vac., the residue was taken up in EA and extracted with KHSO<sub>4</sub> solution, NaHCO<sub>3</sub> solution and water. The organic phase was dried over MgSO<sub>4</sub> and concentrated. The residue was dissolved in a little DCM, precipitated with diethyl ether and filtered off. Yield: 64 mg.

MS (FAB): 1265 (M+Na)<sup>+</sup>, 1243 (M+H)<sup>+</sup>

#### Example 101

N,N'-bis-<(2R-benzyl-3-carboxyl)-propionyl-L-valyl>2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis from example 102 by treatment with trifluoroacetic acid.

MS (FAB): 901 (M+Na)<sup>+</sup>, 879 (M+H)<sup>+</sup>

### Example 102

N,N'-bis-<(2R-benzyl-3-tert.-butoxycarbonyl)-propionyl-L-valyl>-2S,5S-diamino-hexane-3R,4R-diol

45 mg N,N'-bis-<valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride together with 75 mg 2R-benzyl-3-tert.-butoxycarbonyl-propionic acid were dissolved in 2 ml DMF, and 37 mg HOBt, 87 mg TBTU and 112  $\mu$ l ethyldiisopropylamine were added. The solution was stirred for 15 min at RT, the DMF was removed i. vac., the residue was taken up in EA and extracted with KHSO<sub>4</sub> solution, NaHCO<sub>3</sub> solution and water. The organic phase was dried over MgSO<sub>4</sub> and concentrated. The residue was triturated with diethyl ether and filtered off.

Yield: 44 mg.

MS (FAB): 1013 (M+Na)<sup>+</sup>, 991 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $\langle D_6 \rangle$ ): 0.69 (d, 6Hz, 6H); 0.74 (d, 6Hz, 6H); 1.31 (s, 18H); 1.83 (m, 2H); 1.95 (m, 2H); 2.32-2.47 (m, 4H); 2.60-2.87 (m, 6H); 2.98 (m, 2H); 3.29 (m, 2H); 4.09 (dd, 8Hz, 7Hz, 2H); 4.46 (m, 2H); 4.64 (m, 2H); 7.02-7.31 (m, 10H); 7.38 (d, 9Hz, 2H); 7.80 (d, 8Hz, 2H).

The preparation of the carboxy-protected succinic acid derivative in enantiomer-pure form was carried out according to Evans (D. A. Evans, et al., J. Am. Chem. Soc. 104, 1737 (1982); J. J. Plattner, et al., J. Med. Chem. 31, 2277 (1988)).

### Example 103

N,N'-bis-[(3-amino-2-benzyl)-propionyl-L-valyl]-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride (from "diastereomer 1")

Synthesis analogous to example 16 from example 105.

MS (FAB): 843 (M+Na)<sup>+</sup>, 821 (M+H)<sup>+</sup>

### Example 104

N,N'-bis-[(3-amino-2-benzyl)-propionyl-L-valyl]-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride (from "diastereomer 2")

Synthesis analogous to example 16 from example 106.

MS (FAB): 843 (M+Na)<sup>+</sup>, 821 (M+H)<sup>+</sup>

### Example 105

N,N'-bis-[(2-benzyl-3-tert.-butoxycarbonyl-amino)-propionyl-L-valyl]-2S,5S-1,6-diphenyl-hexane-3R,4R-diol (from "diastereomer 1")

37 mg 2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride were coupled with 98 mg N,N'-bis-[(2-benzyl-3-tert.-butoxycarbonyl-amino)-propionyl-L-valine according to the TBTU method. After the usual working up and chromatography 28 mg of product were obtained.

MS (FAB): 1043 (M+Na)<sup>+</sup>, 1021 (M+H)<sup>+</sup>, 921, 821

The building block N,N'-bis-[(2-benzyl-3-tert.-butoxycarbonyl-amino)-propionyl-L-valine was prepared as follows. 2.3 g sodium were dissolved in 170 ml EtOH and 32 ml cyanoacetic ethyl ester were added. 11.5 ml benzylchloride were added by drops with stirring. The solution stood overnight at RT. The NaCl was filtered off and the solvent was distilled off.

The residue was dissolved in EA and extracted with H<sub>2</sub>O. The organic phase was concentrated, the residue was distilled i. vac. (0.5 mm Hg/120-125°C).

Yield: 8.1 g.

The benzylcyanoacetic ethyl ester obtained was dissolved in 200 ml EtOH and hydrogenated over Raney nickel. After suctioning off the catalyst and concentrating, 8.2 g of oil were obtained; after chromatography over silica gel (EA after EA/MeOH 5/1), 5.5 g of 3-amino-2-benzylpropionic ethyl ester.

This compound was reacted with Boc<sub>2</sub>O to 2-benzyl-3-(tert.-butoxycarbonylamino)-propionic ethyl ester, saponified and coupled with H-Val-OMe according to the PPA method. The diastereomers obtained were separated by chromatography (toluene/diisopropyl ether 1/1).

R<sub>f</sub> = 0.140 = diastereomer 1

R<sub>f</sub> = 0.097 = diastereomer 2

Saponification with NaOH in dioxane/water led to the coupling components for examples 105 and 106.

#### Example 106

N,N'-bis-<(2R-benzyl-3-tert.-butoxycarbonyl-amino)-propionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol (from "diastereomer 2")

Synthesis analogous to example 105.

MS (FAB): 1043 (M+Na)<sup>+</sup>, 1021 (M+H), 921, 821

#### Example 107

N,N'-bis-<O-(D-mannofuranosyl)-2S-hydroxy-3-phenyl-propionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

20 mg of the compound from example 108 were stirred for 30 min with methanolic hydrochloric acid at RT. The volatile components were distilled off i. vac., the residue was digested with diethyl ether, suctioned off and dried.

Yield: 13 mg.

NMR (270 MHz, DMSO  $d_6$ ): 0.58 (d, 6Ha, 6H); 0.62 (d, 6Hz, 6H); 1.82 (m, 2H); 2.60 (dd, 4Hz, 14Hz, 2H); 2.71-2.82 (m, 4H); 2.98 (dd, 14Hz, 3Hz, 2H); c. 3.25 (m, 2H); 3.30-3.49 (m, 6H); 3.58 (m, 2H); 3.67 (dd, 11Hz, 3Hz, 2H); c. 3.70-4.30 (m, c. 16H); 4.43 (m, 2H); 4.49 (m, 2H); 7.05-7.29 (m, 20H); 7.35 (d, 9Hz, 2H); 7.67 (d, 9Hz, 2H).

#### Example 107a

N,N'-bis-<O-(2,3-5,6-diisopropylidene-D-mannofuranosyl)-2S-hydroxy-3-phenylpropionyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

57 mg N,N'-bis-<L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride were dissolved with 90 mg O-(2,3-5,6-diisopropylidene-D-mannofuranosyl)-2S-hydroxy-3-phenylpropionic acid in 1 ml DMF and coupled with the TBTU method. Yield: 60 mg.

MS (FAB): 1279 (M+H)<sup>+</sup>, 1261, 1221

NMR (270 MHz, DMSO  $d_6$ ): 0.63 (d, 6Hz, 6H); 0.69 (d, 6Hz, 6H); 1.19 (s, 6H); 1.21 (s, 6H); 1.30 (s, 12H); 1.79 (m, 2H); 2.60-2.82 (m, 8H); 3.29 (m, 2H); 3.73 (dd, 9Hz, 6Hz, 2H); 3.85-3.98 (m, 4H); 4.01-4.18 (m, 4H); 4.23 (dd, 8Hz, 3Hz, 2H); 4.40 (d, 6Hz, 2H); 4.45 (m, 2H); 4.62-4.72 (m, 4H); 7.03-7.32 (m, c. 22H); 7.40 (d, 9Hz, 2H); 7.59 (d, 9Hz, 2H).

O-(2,3-5,6-diisopropylidene-D-mannofuranosyl)-2S-hydroxy-3-phenylpropionic acid was prepared according to R. R. Schmidt from 2,3-5,6-

diisopropylidene-D-mannofuranose and 2S-hydroxy-3-phenyl-propionic acid (R. R. Schmidt and I. Michel; Angew. Chem. 92, 763 (1980); Angew. Chem. Int. Ed. Engl. 19, 731 (1980).

405 mg 0-(2,3-5,6-diisopropylidene-D-mannofuranosyl-trichloroacetimidate together with 194 mg phenyl lactic ethyl ester were dissolved in 15 ml abs.  $\text{CH}_2\text{Cl}_2$ . The solution was cooled to  $0^\circ\text{C}$  and 100  $\mu\text{l}$  of a 1M  $\text{BF}_3$  etherate solution in  $\text{CH}_2\text{Cl}_2$  was added. The solution was permitted to stand for 1 h at  $0^\circ\text{C}$ , was poured into 100 ml  $\text{NaHCO}_3$  solution and extracted with  $\text{CH}_2\text{Cl}_2$ . The organic phase was dried with  $\text{Na}_2\text{SO}_4$  and concentrated. After chromatography with silica gel (mobile solvent: methyl tert.-butyl ether/heptane (1/1)) 195 mg of product were obtained.

#### Example 108

N,N'-bis-(L-phenylalanyl-L-valyl)-3S,6S-diamino-1,8-di(4-pyridyl)-octane-4R,5R-diol tetrahydrochloride

Synthesis analogous to example 16 from 27

MS (FAB): 823 (M+H)<sup>+</sup>

#### Example 109

N,N'-bis-<N-( $\beta$ -D-1-deoxyfructose-1-yl)-L-phenylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol diacetate

69 mg N,N'-bis-<L-phenylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride were suspended with 79 mg D-glucose in 6 ml MeOH and 2 ml pyridine and boiled for 4.5 h. The solvent was removed i. vac., the residue was separated by chromatography over Sephadex LH20 with 10% aqueous acetic acid.

Yield: 71 mg.

MS (FAB): 1139 (M+Na)<sup>+</sup>, 1117 (M+H)<sup>+</sup>

#### Example 110

N,N'-bis-<D-gluconyl-L-phenylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis: treatment of the compound from example 111 with ammonia-saturated methanol.

MS (FAB): 1171 (M+Na)<sup>+</sup>

#### Example 111

N,N'-bis-<2,3,4,5,6-penta-O-acetyl-D-gluconyl-L-phenylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis: by coupling of 2,3,4,5,6-pent-O-acetyl-D-gluconic acid (C. E. Braun and C. D. Cook, Organic Synthesis, vol. 5, 887-889 (1973)) to N,N'-bis-<L-phenylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride with the TBTU method.

MS (FAB): 1569 (M+H)<sup>+</sup>

#### Example 112

N,N'-bis-<tert.-butoxycarbonyl-L-phenylalanyl-L-valyl>-1,4-diamino-butane-2R,3R-diol

Synthesis analogous to example 6 from 1,4-diamino-butane-2R,3R-diol dihydrochloride.

NMR (270 MHz, DMSO  $d_6$ ): 0.83 (d, 6H, 12H); 1.31 (s, 18H); 1.93 (m, 2H); 2.73 (m, 2H); 2.91-3.07 (m, 4H); 3.28 (m, 2H); 3.42 (m, 2H); 4.18 (m,

4H); 4.57 (m, 2H); 7.02 (d, 8Hz, 2H); 7.13-7.32 (m, 10H); 7.66 (d, 8.4Hz, 2H); 8.04 (m, 2H).

MS (FAB): 835 (M+Na)<sup>+</sup>, 813 (M+H)<sup>+</sup>, 713, 613

#### Example 112a

1,4-diamino-butane-2R,3R-diol dihydrochloride

Synthesis from (+)-1,4-di-O-tosyl-2,3-O-isopropylidene-D-threitol  
analogous to examples 2, 2b and 2c.

NMR (60 MHz, DMSO  $\langle D_6 \rangle$ ): 2.9 (m, 4H); 3.73 (m, 2H); c. 5.7-4.5 (br, c. 2H); 8.1 (m, c. 6H).

MS (DCI): 121 (M+H)<sup>+</sup>, 104

#### Example 113

N,N'-bis-<L-phenylalanyl-L-valyl>-1,4-diamino-butane-2R,3R-diol  
dihydrochloride

Synthesis analogous to example 16 from 112.

MS (FAB): 635 (M+Na)<sup>+</sup>, 613 (M+H)<sup>+</sup>

#### Example 114

N,N'-bis<tri-benzyloxycarbonyl-L-arginyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-  
hexane 3R,4R-diol

NMR (270 MHz, DMSO  $\langle D_6 \rangle$ ): 0.71 (d, 7Hz, 12H); 1.57 (m, 8H); 1.80 (m, 2H); 2.73 (m, 2H); 2.94 (m, 2H); 3.30 (m, 2H); 3.70-4.12 (m, 10H); 4.58 (d, 7Hz, 2H); 4.92-5.18 (m, 8H); 5.19 (s, 4H); 7.00-7.42 (m, 40H); 7.49 (d, 8Hz, 4H); 7.64 (d, 8.4Hz, 2H); 9.13 (br.s, 4H).

### Example 115

N,N'-bis-<tert.-butoxycarbonyl-L-cyclohexylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 1005 (M+H)<sup>+</sup>, 905

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.67 (d, 7Hz, 6H); 0.80 (d, 7Hz, 6H) 0.80-1.84 (m, 26H); 1.42 (s, 18H); 2.13 (sept., 7Hz, 2H); 2.80 (dd, 15Hz, 9Hz, 2H); 3.35 (m, 4H); 4.03 (m, 4H); 4.30 (qd, 9Hz, 4Hz, 2H); 4.96 (d, 4Hz, 2H); 6.57 (d, 8Hz, 4H); 7.10-7.30 (m, 12H).

### Example 116

N,N'-bis-<L-cyclohexylalanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

Synthesis analogous to example 16.

MS (FAB): 805 (M+H)<sup>+</sup>, 553, 531

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.79 (d, 7Hz, 6H); 0.85 (d, 7Hz, 6H); 1.00-1.95 (m, 28H); 2.77 (dd, 14Hz, 7Hz, 2H); 2.93 (m, 2H); 3.37 (m, 2H); 3.89 (m, 2H); 4.09 (m 4H); 4.70 (d, 7Hz, 2H); 7.16 (m, 10H); 7.66 (d, 8Hz, 2H); 8.17 (s, 6H); 8.47 (d, 9Hz, 2H).

### Example 117

N,N'-bis-<benzyloxycarbonyl-L-tryptophyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 1139 (M+H)<sup>+</sup>, 720

NMR (270 MHz, DMSO  $<D_6>$ ): 0.75 (m, 12H); 1.96 (m, 2H); 2.76 (dd, 13Hz, 7Hz, 2H); 2.90-3.13 (m, 6H); 3.40 (m, 2H); 4.07 (m, 4H); 4.38 (m, 2H); 4.65 (d, 7Hz, 2H); 4.88 (d, 14Hz, 2H); 4.97 (d, 14Hz, 2H); 6.90-7.35 (m, 28H); 7.47 (d, 8Hz, 2H); 7.58 (d, 8Hz, 2H); 7.65 (d, 8Hz, 2H); 7.83 (d, 8Hz, 2H); 10.80 (s, 2H).

#### Example 118

N,N'-bis-<L-tryptophyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 11.

MS (FAB): 871 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $<D_6>$ ): 0.75 (m, 12H); 1.88 (m, 2H); 2.75 (m, 4H); 2.98 (dd, 14Hz, 2Hz, 2H); 3.13 (dd, 14Hz, 3Hz, 2H); 3.42 (m, 2H); 3.73 (m, 2H); 4.10 (m, 4H); 4.73 (d, 6Hz, 2H); 6.09-7.24 (m, 18H); 7.35 (d, 8Hz, 2H); 7.63 (d, 8Hz, 2H); 7.80 (d, 8Hz, 2H), 8.22 (s, 6H); 10.90 (s, 2H).

#### Example 119

N,N'-bis-<benzyloxycarbonyl-L-1,2,3,4-tetrahydro-isoquinoline-3-yl-carbonyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 1107 (M+Na)<sup>+</sup>, 1085 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $<D_6>$ ): 0.55 (m, 12); 1.70 (m 2H); 2.60-3.81 (m, 10H); 3.90 (m, 2H); 4.03 (m, 2H); 4.38-4.80 (m, 8H); 4.91-5.20 (m, 4H); 7.00-7.53 (m, 28H); 7.58 (d, 8Hz, 2H); 7.72 (d, 8Hz, 2H).

### Example 120

N,N'-bis-<L-1,2,3,4-tetrahydro-isoquinoline-3-yl-carbonyl-L-valyl>2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol diacetate

Synthesis analogous to example 11.

MS (FAB): 839 (M+Na)<sup>+</sup>, 817 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.70 (d, 7Hz, 12H); 1.86 (m, 2H); 1.92 (s, 6H); 2.64-2.89 (m, 4H); 2.92 (dd, 16Hz, 5Hz, 2H); 3.02 (dd, 13Hz, 3Hz, 2H); 3.39 (m, 2H); 3.47 (dd, 9Hz, 5Hz, 2H); 3.90 (s, 4H); 4.03 (m, 2H); 4.10 (dd, 9Hz, 5Hz, 2H); 4.74 (br.s, 2H); 7.02-7.26 (m, 18H); 7.77 (m, 18H); 7.85 (d, 8Hz, 2H).

### Example 121

N,N'-bis-<(2-(benzyl-sulfinyl-methyl)-3-phenyl-propionyl)-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 13.

Synthesis of the building block (2-(benzyl-sulfinyl-methyl)-3-phenyl-propionic acid was accomplished analogous to literature: J. Med. Chem. 3, 1839 (1988).

MA (FAB): 1089 (M+Na)<sup>+</sup>, 1067 (M+H)<sup>+</sup>, 710

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.45 (m, 6H); 0.72 (m, 6H); 1.80 (m, 2H); 2.53-2.95 (m, 12H); 3.22-3.36 (m, 4H); 3.55 (m, 2H); 3.73-4.26 (m, 6H); 4.48 (m, 2H); 7.00-7.40 (m, 30H); 7.85-8.07 (m, 4H).

### Example 122

N,N'-bis-<(2-(p-chlorobenzyl-thio-methyl)-3-phenyl-propionyl)-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 13.

Synthesis of the building block (2-(p-chlorobenzyl-thio-methyl)-3-phenyl-propionic acid was accomplished analogous to literature: J. Med. Chem. 31, 1839 (1988).

MS (FAB): 1125 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.49 (m, 6H); 0.57 (m, 6H); 1.80 (m, 2H); 2.10-2.33 (m, 2H); 2.38-2.60 (m, 4H); 2.62-2.83 (m, 6H); 2.95 (m, 2H); 3.28 (m, 2H); 3.65 (s, 4H); 4.03-4.17 (m, 2H); 4.45 (m, 2H); 4.54-4.67 (m, 2H); 7.00-7.50 (m, 28H); 7.64 (m, 2H); 7.88 (m, 2H).

#### Example 123

N,N'-bis-<(2-(p-chlorobenzyl-sulfonyl-methyl)-3-phenylpropionyl)-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 13.

Synthesis of the building block 2-(p-chlorobenzyl-sulfonyl-methyl)-3-phenyl-propionic acid was accomplished analogous to literature: J. Med. Chem. 31, 1839 (1988).

MS (FAB): 1191 (M+2H+Na)<sup>+</sup> 1189 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.52 (m, 6H); 0.74 (m, 6H); 1.83 (m, 2H); 2.42-2.95 (m, 10H); 3.28-3.54 (m, 6H); 3.90-4.70 (m, 10H); 6.98-7.47 (m, 30H); 8.03 (m, 2H)

#### Example 124

N,N'-bis-<N-tosyl(- $\beta$ -naphthyl-alanyl-L-valyl)>2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 1223 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $\text{d}_6$ ): 0.66 (m, 12H); 1.80 (m, 2H); 2.13 (s, 6H); 2.50-2.90 (m, 8H); 3.30 (m, 2H); 3.98-4.67 (m, 8H); 6.70-8.00 (m, 38H).

### Example 125

N,N'-bis-<N-mesyl- $\beta$ -naphthyl-alanyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 1072 (M+Na)<sup>+</sup>, 838

NMR (270 MHz,  $\text{d}_6$ ): 0.74 (m, 12H); 1.82 (s, 6H); 1.87 (m, 2H); 2.55-3.08 (m, 8H); 3.25 (m, 2H); 4.02 (m, 2H); 4.22 (m, 2H); 4.47 (m, 2H); 4.70 (m, 2H); 7.00-8.00 (m, 30H).

### Example 126

N-<(2R-(1,1-dimethylethyl-sulfonylmethyl)-3-phenylpropionyl)-L-valyl>-N'-<(2S-1,1-dimethylethylsulfonylmethyl)-3-phenyl-propionyl)-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Byproduct from the synthesis of example 52.

Example 126 R<sub>f</sub> = 0.17 (EA)

Example 52 R<sub>f</sub> = 0.35 (EA)

MS (FAB): 1053 (M+Na)<sup>+</sup>

NMR (270 DMSO  $\text{d}_6$ ): 0.47 (d, 7Hz, 3H); 0.48 (d, 7Hz, 3H); 0.70 (d, 7Hz, 3H); 0.75 (d, 7Hz, 3H); 1.14 (s, 9H); 1.27 (s, 9H); 1.82 (m, 2H); 2.60-3.00 (m, c. 10H); 3.08-3.35 (m, c. 3H); 3.38-3.58 (m, 3H); 3.91 (dd, 8Hz, 6Hz, 1H); 4.06 (m, 1H); 4.27 (d, 5Hz, 1H); 4.35-4.54 (m, 3H); 7.00-7.38 (m, 22H); 7.93 (d, 8Hz, 2H); 8.04 (d, 8Hz, 2H).

The following compounds of examples 127-134 were obtained analogous to the syntheses as described in examples 6 or 16.

**Example 127**

N,N'-bis-<tert.-butoxycarbonyl-L-valyl>-2R,5R-diamino-1,6-diphenyl-hexane-3R,4R-diol

MS (FAB): 699 (M+H)<sup>+</sup>, 599, 499

**Example 128**

N,N'-bis-<tert.-butoxycarbonyl-L-valyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

MS (FAB, LiI): 717 (M+Li)<sup>+</sup>

**Example 129**

N,N'-bis-<tert.-butoxycarbonyl-L-cyclohexylglycine>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

MS (FAB): 801 (M+Na)<sup>+</sup>, 779 (M+H)<sup>+</sup>, 679

**Example 130**

N,N'-bis-<tert.-butoxycarbonyl-L-asparaginyI>-2S,5S-diamino-1,6-diophenyl-hexane-3R,4R-diol

MS (FAB): 729 (M+H)<sup>+</sup>, 629

**Example 131**

N,N'-via-<L-valyl>-2S,5S-diamino-1,6-dicyclohexyl-hexane-3S,4S-diol dihydrochloride

**Example 132**

N,N'-bis-<N<sup>6</sup>-benzoxycarbonyl-L-lysyl>-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

**Example 133**

N,N'-bis-<glycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol dihydrochloride

MS (FAB): 415 (M+H)<sup>+</sup>

**Example 134**

N,N-bis-<tert.-butoxycarbonyl-glycyl>-2S,5S-diamino-1,6-diphenyl-hexane-3S,4S-diol

MS (FAB): 615 (M+H)<sup>+</sup>

The following compounds of examples 135-140 were obtained analogous to the syntheses as contained in examples 23 or 24.

**Example 135**

Bis-<N-((N<sup>2</sup>-tert.-butoxycarbonyl-L-lysyl)-L-leucyl)-2S-amino-3-phenyl-propyl>-amine trihydrochloride

MS (FAB): 966 (M+H)<sup>+</sup>

**Example 136**

Bis-<N-(tert.-butoxycarbonyl-2S-amino-3-cyclohexyl-propyl)-amine hydrochloride

MS (FAB): 495 (M+H)<sup>+</sup>

**Example 137**

Bis-<N-(L-leucyl)-2S-amino-3-phenyl-propyl>-amine trihydrochloride

MS (FAB): 510 (M+H)<sup>+</sup>

**Example 138**

Bis-<N-(tert.-butoxycarbonyl-L-leucyl)-2S-amino-3-phenylpropyl>-amine

MS (FAB): 710 (M+H)<sup>+</sup>

**Example 139**

Bis-<2S-amino-3-phenyl-propyl>-amine trihydrochloride

MS (FAB): 284 (M+H)<sup>+</sup>

**Example 140**

Bis-<N-(benzyloxycarbonyl-L-valyl)-2S-amino-3-phenyl-propyl> amine

MS (FAB): 750 (M+H)<sup>+</sup>

**Example 141**

Bis-<N-tert.-butoxycarbonyl-2S-amino-3-methyl-butyl>-amine hydrochloride

Synthesis analogous to example 25.

MS (FAB); 388 (M+H)<sup>+</sup>

**Example 142**

N,N'-bis-<(2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl)-L-valyl>-3S,6S-diamino-1,8-di-(4-pyridyl)-octane-4R<5R diol

Synthesis analogous to example 13 from 27a.

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.83 (m, 12H); 1.14 (s, 18H); 1.66 (m, 2H); 1.82 (m, 2H); 2.00 (m, 2H); 2.50-2.78 (m, 4H); 2.86 (m, 2H); 3.06-3.63 (m,

10H); 4.02 (m, 2H); 4.14 (m, 2H); 4.69 (m, 2H); 7.30-7.60 (m, 14H); 7.74 (d, 8Hz, 2H); 7.87 (m, 2H); 8.16 (m, 2H); 8.32 (d, 8Hz, 2H); 8.58 (m, 4H).

MS (FAB): 1161 (M+H)<sup>+</sup>

#### Example 143

N,N'-bis-<(2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl)-L-valyl>-1,4-diamino-butane-2R,3R-diol

Synthesis analogous to example 13 from 112a.

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.82 (d, 6Hz, 12H); 1.17 (s, 18H); 1.92 (m, 2H); 2.92-3.08 (m, 4H); 3.16-3.53 (m, 10H); 3.53 (dd, 12.8Hz, 8.8Hz, 2H); 4.11 (dd, 8.0Hz, 7.2Hz, 2H); 4.55 (d, 4.8Hz, 2H); 7.38-7.67 (m, 10H); 7.80 (m, 2H); 7.92 (m, 2H); 8.12 (d, 8.4Hz, 2H); 8.20 (d, 8Hz, 2H).

MS (FAB): 973 (M+Na)<sup>+</sup>; 951 (M+H)<sup>+</sup>

#### Example 144

N,N'-bis-<tert.-butoxycarbonyl-L-phenylalanyl-L-valyl>-1,4-diamino-butane

Synthesis analogous to example 6.

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.83 (d, 6Hz, 12H); 1.28 (s, 18H); 1.39 (m, 4H); 1.91 (m, 2H); 2.74 (dd, 12.8Hz, 9.6Hz, 2H); 2.89-3.16 (m, 6H); 4.08-4.23 (m, 4H); 7.02 (d, 8Hz, 2H); 7.14-7.30 (m, 10H); 7.63 (d, 8.4Hz, 2H); 7.95 (m, 2H).

MS (FAB): 781 (M+H)<sup>+</sup>, 681, 581

#### Example 145

N,N'-bis-<l-phenylalanyl-L-valyl>-1,4-diamino-butane dihydrochloride

Synthesis analogous to example 16 from 144.

MS (FAB): 581 (M+H)<sup>+</sup>

#### Example 146

N,N'-bis-[(2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl)-L-valyl]-1,4-diamino-butane

Synthesis analogous to example 13.

NMR (270 MHz, DMSO  $d_6$ ): 0.82 (d, 6H, 12H); 1.19 (s, 18H); 1.32 (m, 4H); 1.89 (m, 2H); 2.98 (m, 4H); 3.32 (m, 2H); 3.42 (m, 6H); 3.54 (dd, 12.8Hz, 8Hz, 2H); 4.04 (t, J=8Hz, 2H); 7.38 (m, 4H); 7.53 (m, 6H); 7.79 (m, 2H); 7.92 (m, 2H); 8.08 (d, 8Hz, 2H); 8.21 (m, 2H).

MS (FAB): 941 (M+Na)<sup>+</sup>, 919 (M+H)<sup>+</sup>

#### Example 147

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-3S,5S-diamino-1,8-diphenyl-octane-4R,5R-diol

Synthesis analogous to example 6 from 3S,6S-diamino-1,8-diphenyl-octane-4R,5R-diol dihydrochloride (latter compound was prepared analogous to examples 2, 2b, 2c and 2e from 1,2R-5R,6-diepoxy-3,4-O-isopropylidene-3R,4R-diol and benzyl lithium).

MS (FAB (LiI)): 1027 (M+Li)<sup>+</sup>, 927, 827

NMR (270 MHz, DMSO  $d_6$ ): 0.88 (m, 12H); 1.28 (s, 18H); 1.57-1.86 (m, 4H); 2.01 (m, 2H); 2.4-2.6 (m, c. 4H); 2.75 (dd, 11Hz, 14Hz, 2H); 2.98 (dd, 14Hz, 4Hz, 2H); 3.32 (m, c. 2H); 4.06-4.26 (m, 4H); 4.32 (dd, 6Hz, 8Hz, 2H); 4.62 (m, 2H); 7.0 (d, 8Hz, 2H); 7.10-7.32 (m, 20H); 7.62 (d, 10Hz, 2H); 7.75 (d, 8Hz, 2H).

#### Example 148

N,N'-bis-(L-phenylalanyl-L-valyl)-3S,6S-diamino-1,8-diphenyl-octane-4R,5R-diol dihydrochloride

Synthesis analogous to example 16 from 147.

MS (FAB): 821 (M+H)<sup>+</sup>, 843 (M+Na)<sup>+</sup>, 803

#### Example 149

N,N'-bis-(<2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl>-L-valyl)-3S,6S-diamino-1,8-diphenyl-octane-4R,5R-diol

Synthesis analogous to examples 13 and 147.

MS (FAB (LiI)): 1165 (M+Li)<sup>+</sup>

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.92 (d, 7Hz, 12H); 1.13 (s, 18H; 1.6-1.85 (m, 4H); 2.04 (m, 2H); 2.40-2.64 (m, 4H); 2.82 (dm, 14Hz, 2H); 3.18 (m, 2H); 3.32-3.52 (m, 6H); 3.58 (m, 2H); 4.08 (m, 2H); 4.22 (t, 8Hz, 2H); 7.1-7.56 (m, 20H); 7.72 (dd, 4Hz, 2H); 7.88 (m, 2H); 8.14 (m, 2H); 8.32 (d, 8Hz, 2H).

#### Example 150

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-6S,9S-diamino-tetradecane-7R,8R-diol

Synthesis analogous to t example 6 from 6S,9S-diamino-tetradecane-7R,8R-diol dihydrochloride (latter compound was prepared analogous to examples 2, 2b, 2c and 2e from 1,2R-5R,6-diepoxy-3,4-0-isopropylidene-3R,4R-diol and n-butyl lithium).

MS (FAB(LiI)): 959 (M+Li)<sup>+</sup>

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.76-0.91 (m, 18H), 1.12-1.54 (m, 16H); 1.28 (s, 18H); 1.98 (m, 18H); 2.74 (dd, 12Hz, 14Hz, 2H); 2.87 (dd, 14Hz, 4Hz, 2H);

3.22 (m, 2H); 3.98 (m, 2H); 4.14-4.32 (m, 4H); 4.46 (s, 2H); 7.0 (d, 8Hz, 2H); 7.14-7.31 (d, 4Hz, 10H); 7.38 (d, 9Hz, 2H); 7.70 (d, 9Hz, 2H).

#### Example 161

N,N'-bis-(L-phenylalanyl-L-valyl)-6S,9S-diamino-tetradecane-7R,8R-diol dihydrochloride

Synthesis analogous to example 16 from 150.

MS (FAB): 753 (M+H)<sup>+</sup>, 775 (M+Na)<sup>+</sup>, 735

#### Example 152

N,N'-bis-(<2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(naphthyl)-propionyl>-L-valyl)-6S,9S-diamino-tetradecane-7R,8R-diol

Synthesis analogous to examples 13 and 150.

MS (FAB (LiI)): 1097 (M+Li)<sup>+</sup>

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.76 (m, 6H); 0.88 (d, 7Hz, 12H); 1.12 (s, 18H); c. 1.10-1.54 (m, 16H); 2.02 (m, 2H); 2.82 (dd, 12Hz, 2Hz, 2H); 3.16 (dd, 12Hz, 16Hz, 2H); 3.24 (m, 2H); 3.36-3.52 (m, 4H); 3.58 (dd, 8Hz, 13Hz, 2H); 3.98 (m, 2H); 4.16 (t, 6Hz, 2H); 4.44 (s, 2H); 7.18 (d, 10Hz, 2H); 7.42-7.48 (m, 4H); 7.49-7.62 (m, 4H); 7.81 (m, 2H); 7.92 (m, 2H); 8.20 (d, 8Hz, 2H); 8.30 (d, 8.4Hz, 2H).

#### Example 153

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-valyl)-2S,5S-diamino-1,8-bis-(3,4-methylenedioxyphenyl)-hexane-3R,4R-diol

Synthesis analogous to example 6 from 2S,5S-diamino-1,6-bis-(3,4-methylenedioxyphenyl)-hexane-3R,4R-diol dihydrochloride (latter compound was

prepared analogous to examples 2, 2b, 2c and 2e from 1,2R-5R,6-diepoxy-3,4-O-isopropylidene-3R,4R-diol and 3,4-methylenedioxyphenyl lithium).

MS (FAB): 1103 (M+Na)<sup>+</sup>, 1081 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.73 (d, 6Hz, 6H); 0.76 (d, 6Hz, 6H); 1.28 (s, 18H); 1.87 (m, 2H); 2.52-2.78 (m, 6H); 2.91 (dd, 14Hz, 4Hz, 2H); 3.26 (m, 2H); 4.11-4.22 (m, 4H); 4.35 (m, 2H); 4.66 (m, 2H); 5.84 (s, 2H); 5.86 (s, 2H); 6.63 (d, 8Hz, 2H); 6.69 (d, 8Hz, 2H); 6.75 (s, 2H); 6.99 (d, 9Hz, 2H); 7.13-7.33 (m, 10H); 7.45 (d, 9Hz, 2H); 7.59 (d, 9Hz, 2H).

#### Example 154

N,N'-bis-(L-phenylalanyl-L-valyl)-2S,5S-diamino-1,6-bis-(3,4-methylenedioxyphenyl)-hexane-3R,4R-diol dihydrochloride

Synthesis analogous to example 16 from 153.

MS (FAB): 881 (M+H)<sup>+</sup>, 863

#### Example 155

N,N'-bis-(<2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl>-L-valyl)-2S,5S-diamino-1,6-bis-(3,4-methylenedioxy-phenyl)-hexane-3R,4R-diol

Synthesis analogous to examples 13 and 153.

MS (FAB); 1241 (M+Na)<sup>+</sup>, 1219 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO <D<sub>6</sub>>): 0.73 (d, 7Hz, 6H); 0.78 (d, 7Hz, 6H); 1.10 (s, 18H); 1.89 (m, 2H); 2.55-2.72 (m, 4H); 2.79 (dm, 14Hz, 2H); 3.08 (dd, 14Hz, 10Hz, 2H); c. 3.22-3.43 (m, c. 6H); 3.58 (dd, 14Hz, 10Hz, 2H); 4.07 (m, 2H); 4.45 (m, 2H); 4.49 (m, 2H); 5.75 (s, 2H); 5.78 (s, 2H); 6.68 (s, 2H); 6.80 (s, 2H); 7.25 (d, 9Hz, 2H); 7.39-7.45 (m, 4H); 7.54 (m, 6H); 7.80 (m, 2H); 7.92 (m, 2H); 8.15-8.25 (m, 4H).

#### Example 156

N,N'-bis-( $\alpha$ -(1,1-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl)-L-isoleucyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 13.

MS (FAB): 1181 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $d_6$ ): 0.63 (d, 7Hz, 6H); 0.73 (t, 7Hz, 6H); 0.99 (m, 2H); 1.11 (s, 18H); 1.32 (m, 2H); 1.64 (m, 2H); 2.63-2.88 (m, 6H); 3.07 (dd, 15Hz, 11Hz, 2H); c. 3.28-3.43 (m, c. 6H); 3.58 (dd, 14Hz, 9Hz, 2H); 4.09 (t, 8Hz, 2H); 4.48-4.62 (m, 4H); 7.03 (m, 2H); 7.12-7.31 (m, 10H); 7.43 (m, 4H); 7.54 (m, 4H); 7.81 (m, 2H); 7.92 (m, 2H); 8.15-8.25 (m, 4H).

#### Example 157

N,N'-bis-(N<sup>2</sup>-( $\alpha$ -hexadecyl-sulfonyl)-L-lysyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to examples 11 and 58.

MS (FAB): 1330 (M+H)<sup>+</sup>

#### Example 158

N,N'-bis-(N<sup>2</sup>-( $\alpha$ -tetradecanoyl)-L-lysyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to examples 11 and 58.

MS (FAB): 1174 (M+H)<sup>+</sup>

#### Example 159

N,N'-bis-(tert.-butoxycarbonyl-L-phenylalanyl-L-asparaginy)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 6.

MS (FAB): 1045 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $d_6$ ): 1.27 (s, 18H); 2.20-2.78 (m, 10H); 2.90 (m, 2H); 3.30 (m, 2H); 4.14 (m, 2H); 4.28 (m, 2H); 4.45 (m, 2H); 4.64 (s, 2H); 6.88 (s, 4H); 7.02-7.37 (m, 24H); 8.04 (d, 8Hz, 2H).

#### Example 160

N,N'-bis-(L-phenylalanyl-L-asparaginy)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 16 from 159.

MS (FAB): 823 (M+H)<sup>+</sup>

#### Example 161

N,N'-bis-(2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(naphthyl)-propionyl-L-asparaginy)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 13.

MS (FAB): 1183 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $d_6$ ): 1.17 (s, 18H); 2.22 (m, 2H); 2.37-2.76 (m, 10H); 2.90 (m, 2H); 3.25 (m, 4H); 3.58 (m, 2H); 4.25 (m, 2H); 4.40 (m, 2H); 4.62 (m, 2H); 6.93-7.60 (m, 24H); 7.77 (m, 2H); 7.90 (m, 2H); 8.22 (d, 8Hz, 2H); 8.33 (d, 8Hz, 2H).

#### Example 162

N,N'-bis-(2-(1,1-dimethylethyl-sulfonylmethyl)-3-(4-pyridyl)-propionyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol dihydrochloride

Synthesis analogous to example 13.

2-(1,1-dimethylethyl-sulfonylmethyl)-3-(4-pyridyl)-propionic acid was used as racemate in the coupling; the diastereomer products were separated chromatographically.

Rf values: mobile solvent acetic ester/methanol/glacial acetic acid 60/40/1.

a) Rf = 0.50

b) Rf = 0.44

c) Rf = 0.33

MS (FAB):

a) isomer 1: 1055 (M+Na)<sup>+</sup> 1033 (M+H)<sup>+</sup>

b) isomer 2: 1055 (M+Na)<sup>+</sup> 1033 (M+H)<sup>+</sup>

c) isomer 3: 1055 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $\langle D_6 \rangle$ ):

a) isomer 1: 0.68 (d, 7Hz, 6H); 0.74 (d, 7Hz, 6H); 1.19 (s, 18H); 1.83 (m, 2H); 2.53-2.94 (m, 10H); c. 3.2-3.45 (m, c. 10H); 3.53 (dd, 14Hz, 9Hz, 2H); 4.06 (dd, 9Hz, 7Hz, 2H); 4.52 (m, 2H); 7.05 (m, 2H); 7.10-7.25 (m, 8H); 7.28 (d, 5Hz, 4H); 7.53 (d, 9Hz, 2H); 8.19 (d, 9Hz, 2H); 8.46 (d, 8Hz, 4H)

b) isomer 2: 0.38, 0.44, 0.65, 0.73 (d, each 7Hz, each 3H), 1.18, 1.28 (2s, each 9H); 1.70-1.88 (m, 2H); 2.54-3.05 (m, c. 11H); 3.15-3.60 (m, c. 10H); 3.87 (dd, 8Hz, 6Hz, 2H); 4.03 (dd, 9Hz, 7Hz, 1H); 4.36-4.52 (m, 2H); c. 4.4-5.0 (1H); 7.00-7.30 (m, 14H); 7.41, 7.58, 8.18, 8.27 (4d, each 9Hz, each 1H); 8.43, 8.46 (2d, each 6Hz, each 1H)

c) isomer 3: 0.34 (d, 7Hz, 6H); 0.40 (d, 7Hz, 6H); 1.31 (s, 18H); 1.73 (m, 2H); 2.60-3.07 (m, 12H); 3.28 (s, 2H); 3.38-3.58 (m, 4H); 3.81 (dd, 8Hz, 6Hz, 2H); 4.42 (m, 2H); c. 4.3-5.3 (2H); 7.03-7.30 (m, 14Hz), 7.43 (d, 9Hz, 2H); 8.28 (d, 9Hz, 2H); 8.43 (d, 6Hz, 4H).

### Example 163

N,N'-bis-( $\leq$ 2-(1,1-dimethylethyl-sulfonylmethyl)-3-(N-oxido-4-propionyl>L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 162.

2-(1,1-dimethylethyl-sulfonylmethyl)-3-(N-oxido-4-pyridyl)-propionic acid comes from the preliminary stage 2-(1,1-dimethylethyl-thio-methyl)-3-(4-pyridyl)-propionic acid through oxidation with three instead of two equivalents of potassium peroxymonosulfate (Oxone<sup>R</sup>) as in example 162.

MS (FAB): 1065 (M+H)<sup>+</sup>

### Example 164

N,N'-bis-( $\leq$ bis-(1,1-dimethylethyl-thio-methyl)-acetyl>L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 13. The synthesis of the bis-(1,1-dimethylethyl-thio-methyl)-acetic acid was accomplished from bis-(hydroxymethyl)-maleic diethyl ester by reaction with hydrogen bromide and subsequent substitution of the B,B'-dibromoisobutyric acid with potassium tert.-butyl sulfide.

MS (FAB): 990 (M+H)<sup>+</sup>

NMR (270 MHz, CDCl<sub>3</sub>): 0.59 (d, 7Hz, 6H); 0.85 (d, 7Hz, 6H); 1.29 (s, 18H); 1.33 (s, 18H); 2.16 (m, 2H); 2.42 (m, 2H); 2.70-3.02 (m, 14H); 3.48 (br.s, 2H); 4.13 (m, 2H); 4.28 (m, 2H); 5.33 (d, 8Hz, 2H); 6.47 (d, 8Hz, 2H); 7.20-7.28 (m, 10H).

#### Example 165

N,N'-bis-(bis(-1,1-dimethylethyl-sulfonylmethyl)-acetyl>L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to examples 164 and 13.

MS (FAB): 1118 (M+H)<sup>+</sup>

#### Example 166

N,N'-bis-(1-naphthyl>-acetyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 58.

MS (FAB): 834 (M+H)<sup>+</sup>

#### Example 167

N,N'-bis-(1-naphthyloxy>-acetyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 58.

MS (FAB): 866 (M+H)<sup>+</sup>

#### Example 168

N,N'-bis-(2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl>L-valyl)-2S,5S-diamino-1,6-bis-(4-tert.-butylphenyl)-hexane-3R-4R-diol

Synthesis analogous to example 6 from 2S,5S-diamino-1,6-bis-(tert.-butylphenyl)-hexane-3R,4R-diol dihydrochloride (latter compound was prepared analogous to examples 2, 2b, 2c and 2e from 1,2-R-5R,6-diepoxy-3,4-O-isopropylidene-3R,4R-diol and 4-tert.-butylphenyl lithium).

MS (FAB): 1265 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $d_6$ ): 0.67 (d, 7Hz, 6H); 0.76 (d, 7Hz, 6H); 1.09 (s, 18H); 1.11 (s, 18H); 1.87 (m, 2H); 2.60-2.85 (m, 6H); 3.08 (dd, 14Hz, 12Hz, 2H); 3.25-3.50 (m, 8H); 3.60 (dd, 14Hz, 9Hz, 2H); 4.06 (m, 2H); 4.52 (m, 2H); 7.10-7.22 (m, 8H); 7.27 (d, 9Hz, 2H); 7.34-7.62 (m, 8H); 7.80 (m, 2H); 7.92 (m, 2H); 8.22 (d, 8Hz, 4H).

#### Example 169

N,N'-bis-( $\langle$ 2S-(1,1-dimethylethyl-sulfonylmethyl)-3-(1-naphthyl)-propionyl>L-valyl)-2S,5S-diamino-1,6-bis-(2,4-dimethoxyphenyl)-hexane-3R,4R-diol

Synthesis analogous to example 6 from 2S,5S-diamino-1,6-bis-(2,4-dimethoxyphenyl)-hexane-3R,4R-diol dihydrochloride (latter compound was prepared analogous to examples 2, 2b, 2c and 2e from 1,2R-5R,6-diepoxy-3,4-O-isopropylidene-3R,4R-diol and 2,4-dimethoxyphenyl lithium).

MS (FAB): 1250 (M+H)<sup>+</sup>

#### Example 170

N,N'-bis-(2- $\langle$ 4-pyridyl>ethylsulfonyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 58.

MS (FAB): 836 (M+H)<sup>+</sup>

#### Example 171

N,N'-bis-(12-amino-dodecanoyl-L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 58.

MS (FAB): 892 (M+H)<sup>+</sup>

### Example 172

N,N'-bis-( $\langle$ 2-quinolylcarbonyl $\rangle$ -L-valyl)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 58.

MS (FAB): 831 (M+Na)<sup>+</sup>, 809 (M+H)<sup>+</sup>

NMR (270 MHz, DMSO  $\langle$ D<sub>6</sub> $\rangle$ ): 0.80 (d, 7Hz, 6H), 0.84 (d, 7Hz, 6H); 2.65 (dd, 14Hz, 4Hz, 2H); 2.83 (dd, 14Hz, 10Hz, 2H); 3.34 (m, 2H); 4.43 (dd, 6Hz, 9Hz, 2H); 4.55 (m, 2H); 4.80 (m, 2H); 6.86 (m, 2H); 7.07 (t, 8Hz, 4H); 7.22 (d, 8Hz, 4H); 7.74 (m, 2H); 7.89 (m, 4H); 7.89 (m, 4H); 8.12 (d, 8Hz, 2H); 8.19 (m, 4H); 8.57 (d, 9Hz, 2H); 8.61 (d, 9Hz, 2H).

### Example 173

N,N'-bis-( $\langle$ 2-quinolylcarbonyl $\rangle$ -L-asparaginyI)-2S,5S-diamino-1,6-diphenyl-hexane-3R,4R-diol

Synthesis analogous to example 58.

MS (FAB): 861 (M+Na)<sup>+</sup>

NMR (270 MHz, DMSO  $\langle$ D<sub>6</sub> $\rangle$ ): 2.33-2.78 (m, 8H); 3.30 (m, 2H); 4.33 (m, 2H); 4.70 (m, 4H); 4.70 (m, 4H); 6.80-8.22 (m, 26H); 8.59 (d, 8Hz, 2H); 8.92 (d, 8Hz, 2H).

### Example 174

N,N'-bis-(tert-butoxycarbonyl)-2S,4-diamino-1,5-diphenyl-pentane-3-ol

2.3 g tert.-butoxycarbonyl-L-phenylalanyl were dissolved in 10 ml ethanol. After addition (at 0°C) of 0.05 ml tetramethyl guanidine and a solution of 2.42 g 2-nitro-1-phenyl ethane in 2 ml ethanol the solution was

permitted to warm to RT and stand overnight. The solution was concentrated, the remaining light oil (4.8 g) was used again directly.

4.7 g of the oil obtained above were dissolved in 70 ml ethanol. After the addition of 0.1 ml glacial acetic acid and 1 g Raney nickel the solution was shaken for 16 h at 50°C and 25 atm. hydrogen in a glass insert in the autoclave. The catalyst was filtered off; the eluate was evaporated to an oil. The residue was dissolved in water/1N HCl and extracted 4 times with acetic ester. The acetic ester extract was concentrated and used again directly (2.6 g).

2.57 g of the amino compound obtained above were dissolved in 25 ml dioxane at RT. After addition of 0.86 ml triethyl amine and 1.7 g di-tert.-butyldicarbonate the solution was stirred for another 30 min. The solution was concentrated and ice water, acetic ester and  $\text{KHSO}_4$  were added up to pH 2. The acetic ester phase was washed with aqueous NaCl solution, dried over  $\text{Na}_2\text{SO}_4$  and concentrated. 3.3 g of an oil were obtained. This was further refined by chromatography on silica gel ( $\text{CH}_2\text{Cl}_2$ /methanol/glacial acetic acid 100/3/0.3). 2.2 g of product were obtained as a mixture of the diastereomers.

MS (FAB): 471 (M+H)<sup>+</sup>, 371, 315

### Example 175

N,N'-bis-(tert.-butoxycarbonyl)-1,3-diaminopropane

MS (FAB): 495 (M+Na)<sup>+</sup>, 473 (M+H)<sup>+</sup>

NMR (270 MHz,  $\text{CDCl}_3$ ): 0.97 (dd, 12H); 1.45 (s, 18H); 1.70 (t, 6Hz, 2H); 2.03 (m, 2H); 3.08 (m, 2H); 3.58 (m, 2H); 3.88 (dd, 2H); 5.09 (d, 2H); 7.21 (s, 2H).

### Example 176

N,N'-bis-(tert.-butoxycarbonyl)-1,3-diaminopropane-2-ol.

MS (FAB/LiCl): 495 (M + Li)<sup>+</sup>

NMR (270 MHz, CDCl<sub>3</sub>): 0.97 (dd, 12H); 1.45 (s, 18H); 2.04 (m, 2H); 3.20 (m, 2H); 3.61 (m, 2H); 3.90 (dd, 2H); 3.95 (m, 1H); 5.16 (dd, 2H); 7.18 (s, 1H); 7.49 (s, 1H).

### Example 177

N,N'-bis-(tert.-butoxycarbonyl)-1,3-diaminoacetone

MS (FAB/LiCl): 493 (M+Li)<sup>+</sup>

NMR (270 MHz, CDCl<sub>3</sub>): 0.98 (dd, 12H); 1.45 (s, 18H); 2.09 (m, 2H); 3.94 (dd, 2H); 4.10 (s, 2H); 4.18 (s, 2H); 5.20 (d, 2H); 7.50 (s, 2H).

### Example 178

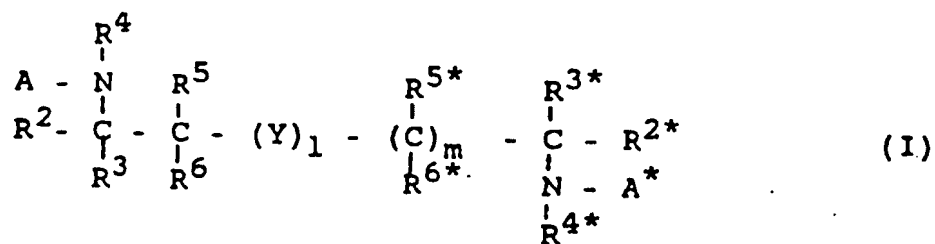
N,N'-bis-(tert.-butoxycarbonyl)-1,4-diaminobutane-2-on

MS (FAB): 523 (M+Na)<sup>+</sup>, 501 (M+H)<sup>+</sup>

NMR (270 MHz, CDCl<sub>3</sub>): 0.95 (m, 12H); 1.43 (d, 18H); 2.09 (m, 2H); 2.69 (m, 2H); 3.45 (m, 1H); 3.86 (m, 1H); 3.90 (m, 1H); 3.99 (m, 1H); 4.18 (m, 1H); 5.23 (d, 2H); 6.91 (s, 1H); 7.17 (s, 1H).

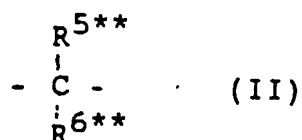
### Claims

1. Compound of formula I



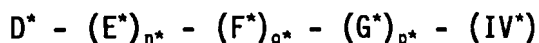
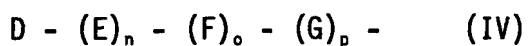
wherein

Y stands for oxygen, sulfur a radical of formula II or a radical of formula III



l and m, independent of each other, are 0 or 1;

A means a radical of formula IV and A\* a radical of formula IV\*



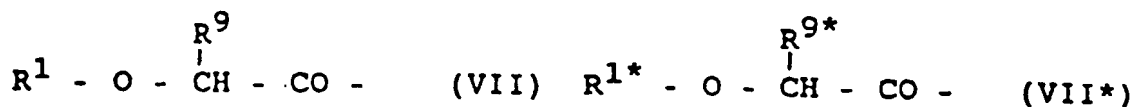
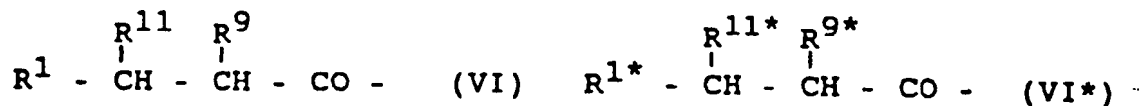
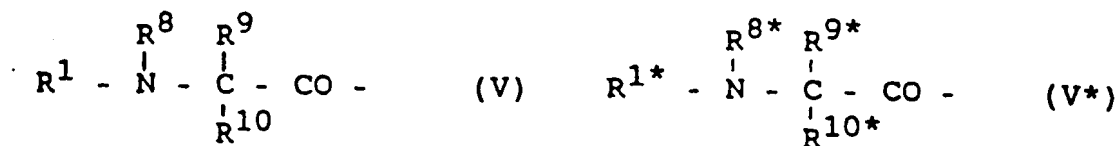
where

E, E\*, F, F\*, G and G\*, independent of one another, stand for a natural or an unnatural amino acid, azaamino acid or imino acid;

n, n\*, o, o\*, p and p\*, independent of one another, mean 0 or 1;

D stands for R<sup>1</sup> or a radical of formulas V, VI or VII, and

D\* stands for R<sup>1\*</sup> or a radical of formulas V\*, VI\* or VII\*



and wherein  $R^1$  and  $R^{1*}$ , independent of each other, stand for

$a_1$ )

- hydrogen
- carboxyl.
- $(C_1-C_{18})$ -alkyl, which may be simply or doubly unsaturated and which may be substituted by up to 3 identical or different radicals from the series
- mercapto,
- hydroxy,
- $(C_1-C_7)$ -alkoxy,
- carbamoyl
- $(C_1-C_8)$ -alkanoyloxy,
- carboxy,
- $(C_1-C_7)$ -alkoxycarbonyl,
- F, Cl, Br, I,
- amino
- amidino, which if appropriate can be substituted by one, two or three  $(C_1-C_8)$ -alkyl radicals,

- guanidino, which if appropriate can be substituted by one or two benzyloxycarbonyl radicals or by one, two, three or four (C<sub>1</sub>-C<sub>8</sub>)-alkyl radicals,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino,
- (C<sub>7</sub>-C<sub>15</sub>)-aralkoxycarbonyl,
- (C<sub>7</sub>-C<sub>15</sub>)-aralkoxycarbonylamino,
- Phenyl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- 9-fluorenylmethoxycarbonylamino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylsulfinyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylthio,
- hydroxamino,
- hydroximino,
- sulfamoyl,
- sulfo,
- carboxamido,
- formyl,
- hydrazono,
- imino,
- a radical CONR<sup>12</sup>R<sup>13</sup> or CONR<sup>12\*</sup>R<sup>13\*</sup>,
- by up to six hydroxy or
- by up to five (C<sub>1</sub>-C<sub>8</sub>)-alkanoxyloxy;
- mono-, bi- or tri-cyclic (C<sub>3</sub>-C<sub>18</sub>)-cycloalkyl,

- (C<sub>3</sub>-C<sub>18</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, the cycloalkyl part in each case being substituted if appropriate by one or two identical or different radicals from the series

- F, Cl, Br, I,
- carboxy,
- carbamoyl,
- carboxymethoxy,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyloxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylamino-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- di-(C<sub>1</sub>-C<sub>6</sub>)-alkylamino-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- amidino,
- hydroxamino,
- hydroximino,
- hydrazono,
- imino,
- guanidino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxysulfonyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxysulfinyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino
- (C<sub>6</sub>-C<sub>12</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino and

- trifluoromethyl;
- (C<sub>6</sub>-C<sub>14</sub>)-aryl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryloxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl or
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl, wherein the aryl part in each case is substituted if appropriate by one, two or three identical or different radicals from the series
- F, Cl, Br, I,
- hydroxy,
- mono-, di- or tri-hydroxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- trifluoromethyl,
- formyl,
- carboxamido,
- mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylaminocarbonyl,
- nitro,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- carboxy,
- carboxymethoxy,
- amino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,

- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonylmethoxy,
- carbamoyl,
- sulfamoyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxysulfonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkylsulfonyl,
- sulfo-(C<sub>1</sub>-C<sub>8</sub>)-alkyl
- guanidino (C<sub>1</sub>-C<sub>8</sub>)-alkyl and
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino;
- het,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,
- het-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- het-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkoxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- het-thio-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-thio-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,
- het-thio-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,

where in each case het stands for the radical of a 5- to 7-member monocyclic or 8- to 10-member bicyclic ring system which can be benzannellated, aromatic, partly hydrogenated or completely hydrogenated, which can contain as heteroelements one, two, three or four different radicals from the group N, O, S, NO, SO, SO<sub>2</sub>, which can be substituted with 1 to 6 hydroxy and which, if appropriate, is mono-, di- or tri-substituted as defined for (C<sub>6</sub>-C<sub>14</sub>)-aryl under a<sub>1</sub>) and/or with oxo,

or mean a radical NR<sup>12</sup>R<sup>13</sup> or NR<sup>12\*</sup>R<sup>13\*</sup>,

or

a<sub>2</sub>)

- a radical of formula VIII or VIII\*

$R^{1a}-W$  (VIII)

$R^{1a*}-W^*$  (VIII\*)

wherein  $R^{1a}$  and  $R^{1a*}$  are defined like  $R^1$  and  $R^{1*}$  under  $a_1$ ) and  $W$  and  $W^*$  stand for  $-CO-$ ,  $-CS-$ ,  $O-CO-$ ,  $-SO_2-$ ,  $-SO-$ ,  $-S-$ ,  $-NHSO_2-$ ,  $-NHCO-$ ,  $-CH(OH)-$ ,  $N(OH)-$  or  $-CO-V-$  with  $V$  meaning a peptide with 1 to 10 amino acids;

or wherein  $R^1$  and  $R^{1*}$ , independent of each other, together with  $R^{11}$  or  $R^{12}$  and the atoms that carry them form monocyclic or bicyclic, saturated or partly unsaturated ring systems with 5-12 ring members which in addition to carbon can also contain 1 sulfur atom, which may be oxidized to sulfoxide or sulfone;  
 $a_3$ )

- a glycosyl radical, preferably a glucofuranosyl or glucopyranosyl radical, which is derived from naturally occurring aldotetroses, aldopentoses, aldohexoses, ketopentoses, ketohexoses, desoxyaldoses, aminoaldoses and oligosaccharides as well as their stereoisomers;

$R^2$  and  $R^{2*}$

are defined independent of each other like  $R^1$  and  $R^{1*}$  under  $a_1$ ) or  $a_2$ ) or together with  $R^4$  or  $R^{4*}$  and the atoms carrying them form mono- or bicyclic, saturated or partly unsaturated ring systems with 5 to 12 ring members, or together with  $R^3$  or  $R^{3*}$  and the atoms carrying them form cyclic, saturated or partly unsaturated ring systems with 3 to 12 ring members;

$R^3$  and  $R^{3*}$

independent of each other mean

- hydrogen or

-  $(C_1-C_3)$ -alkyl;

$R^4$  and  $R^{4*}$ ,

independent of each other, mean

- hydrogen or
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl;

R<sup>5</sup>, R<sup>5\*</sup> and R<sup>5\*\*</sup>,

independent of one another, mean

- hydrogen.
- hydroxy,
- amino or
- carboxy, or

with R<sup>6</sup>, R<sup>6\*</sup> or R<sup>6\*\*</sup> together with the carbon atoms carrying these, in each case independent of one another, form a keto group;

R<sup>6</sup>, R<sup>6\*</sup> and R<sup>6\*\*</sup>,

independent of one another, mean

- hydrogen or
- (C<sub>1</sub>-C<sub>6</sub>)-alkyl or

in the case of l=0, R<sup>6</sup> and R<sup>6\*</sup> can possibly form a common bond;

R<sup>7</sup> means

- hydrogen,
- hydroxy or
- (C<sub>1</sub>-C<sub>6</sub>)-alkyl;

R<sup>8</sup> and R<sup>8\*</sup>,

independent of each other, mean

- hydrogen or
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl, or together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form mono- or bicyclic, saturated or partly unsaturated ring systems with 5 to 12 ring members;

$R^9$  and  $R^{9*}$

independent of each other are defined like  $R^1$  or  $R^{1*}$  under  $a_1$ ), stand for hydroxy or  $(C_1-C_4)$ -alkanoyloxy, or together with  $R^{10}$  or  $R^{10*}$  and the atoms carrying these form cyclic, saturated or partly unsaturated ring systems with 3 to 12 ring members;

or

together with  $R^{11}$  or  $R^{11*}$  and the atoms carrying these form a mono- or bicyclic, saturated or partly unsaturated ring system with 5-12 ring members, which in addition to carbon can also contain 1 sulfur atom, which possibly can be oxidized to sulfoxide or sulfone; or can contain 1 nitrogen atom, the ring system possibly being substituted by amino;

$R^{10}$  and  $R^{10*}$ ,

independent of each other, mean

- hydrogen or
- $(C_1-C_6)$ -alkyl;

$R^{11}$  and  $R^{11*}$ ,

independent of each other, mean

- hydrogen,
- hydroxy,
- $(C_1-C_4)$ -alkanoyloxy or
- $(C_1-C_8)$ -alkyl;

$R^{12}$ ,  $R^{12*}$ ,  $R^{13}$  and  $R^{13*}$ ,

independent of one another, mean

- hydrogen,
- $(C_1-C_8)$ -alkyl which can be substituted by
- amino,

- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- mercapto,
- carboxy,
- hydroxy or
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>3</sub>-C<sub>7</sub>)-cycloalkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl, (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl which in the aryl part can be substituted as described for R<sup>1</sup> or R<sup>1\*</sup>,
- het or
- het-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, het being defined as described for R<sup>1</sup> or R<sup>1\*</sup>,

or where R<sup>12</sup> and R<sup>13</sup> or R<sup>12\*</sup> and R<sup>13\*</sup> together with the nitrogen atoms carrying these form monocyclic or bicyclic, saturated, partly unsaturated or aromatic ring systems which in addition to carbon can also contain 1 or 2 nitrogen atoms, 1 sulfur atom or 1 oxygen atom as further ring members and which can be substituted by

(C<sub>1</sub>-C<sub>4</sub>)-alkyl,

where

in the compounds of formula I cited above, one or more amide groups (-CONH-) of the main chain can be replaced by -CH<sub>2</sub>NR<sup>14</sup>-, -CH<sub>2</sub>S-, -CH<sub>2</sub>O-, -OCH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH=CH-(cis and trans), -COCH<sub>2</sub>-, -CH(OH)CH<sub>2</sub>-, -CH<sub>2</sub>SO-, -CH<sub>2</sub>SO<sub>2</sub>-, -COO-, -P(O)(OR<sup>15</sup>)CH<sub>2</sub>- and -P(O)(OR<sup>15</sup>)NH-, or also by an amide group with reversed polarity (-NHCO-);

wherein R<sup>14</sup> and R<sup>15</sup>,

independent of each other, stand for

- hydrogen or
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

as well as their physiologically tolerated salts.

2. Compound of formula I according to claim 1, characterized in that the radicals and symbols with and without asterisk are in each case identical.

3. Compound of formula I according to claims 1 and 2, characterized in that the compound is C<sub>2</sub>-symmetrical.

4. Compound of formula I according to claims 1-3, characterized in that

Y stands for a radical of formula II or a radical of formula II;

l, m, A, A\*, D, D\*, n, n\*, o, o\*, p and p\* are defined as in claim 1;

E, E\*, F, F\*, G and G\*, independent of each other, stand for a natural or unnatural  $\alpha$ -amino acid or  $\alpha$ -imino acid;

R<sup>1</sup> and R<sup>1\*</sup>,

independent of each other, stand for

a<sub>1</sub>) - hydrogen,

- carboxyl,

- (C<sub>1</sub>-C<sub>16</sub>)-alkyl, which may be simply saturated and which may be substituted by up to 2 identical or different radicals from the series

- hydroxy,

- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,

- carbamoyl,

- (C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy,

- carboxy,

- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,

- F,

- amino,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino,
- benzyloxycarbonyl,
- benzyloxycarbonylamino,
- 9-fluorenylmethoxycarbonylamino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfonyl,
- a radical CONR<sup>12</sup>R<sup>13</sup> or CONR<sup>12\*</sup>R<sup>13\*</sup>,
- by up to six hydroxy or
- by up to four (C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy;
- mono- or bicyclic (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl where in each case the cycloalkyl part is substituted by one or two identical or different radicals from the series
- F,
- carboxy,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyloxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino,
- benzyloxycarbonylamino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino and
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino;
- (C<sub>6</sub>-C<sub>10</sub>)-aryl,

- (C<sub>6</sub>-C<sub>10</sub>)-aryloxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl or
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, wherein the alkyl part in each case is possibly substituted by one, two or three identical or different radicals from the series
- F, Cl, Br,
- hydroxy,
- hydroxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- carboxamido,
- mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylaminocarbonyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- carboxy,
- carbamoyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino;
- het,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-(C<sub>5</sub>-C<sub>6</sub>)-cycloalkyl,
- het-thio-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- het-thio-(C<sub>5</sub>-C<sub>6</sub>)-cycloalkyl,

where het in each case stands for a 5- to 6-member monocyclic or 8- to 10-member bicyclic ring system which can be aromatic, partly hydrogenated or completely hydrogenated, which can contain as heteroelements one, two, three

of four different radicals from the group N, O, S, NO, SO, SO<sub>2</sub>, which can be substituted with 1 to 4 hydroxy and which can possibly be mono- or di-substituted as defined for (C<sub>6</sub>-C<sub>10</sub>)-aryl under a<sub>1</sub>) and/or with oxo,

or means a radical NR<sup>12</sup>R<sup>13</sup> or NR<sup>12\*</sup>R<sup>13\*</sup> or,

a<sub>2</sub>) - a radical of formula VIII or VIII\*

R<sup>1a</sup> - W (VIII)

R<sup>1a\*</sup> - W\* (VIII\*)

wherein R<sup>1a</sup> and R<sup>1a\*</sup> are defined like R<sup>1</sup> and R<sup>1\*</sup> under a<sub>1</sub>) and W or W\* stand for -CO-, -O-CO-, -SO<sub>2</sub>-, -SO-, -S-, -NHCO- OR -CH(OH)-;

or wherein R<sup>1</sup> and R<sup>1\*</sup> independent of each other together with R<sup>11</sup> or R<sup>11\*</sup> and the atoms carrying these form monocyclic, saturated or partly unsaturated ring systems with 5-8 ring members, which in addition to carbon also can contain 1 sulfur atom, which can possibly be oxidized to sulfoxide or sulfone;

a<sub>3</sub>) - a glycosyl radical that is defined as in claim 1;

R<sup>2</sup> and R<sup>2\*</sup>,

independent of each other, mean

b<sub>1</sub>) hydrogen,

- carboxy,

- (C<sub>1</sub>-C<sub>10</sub>)-alkyl which is possibly simply or doubly unsaturated and which is possibly substituted by up to 3 identical or different radicals from the series

-hydroxy,

- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,

- (C<sub>1</sub>-C<sub>7</sub>)-alkylthio,

- (C<sub>1</sub>-C<sub>7</sub>)-alkylsulfinyl,

- (C<sub>1</sub>-C<sub>7</sub>)-alkylsulfonyl,

- (C<sub>1</sub>-C<sub>7</sub>)-alkanoyloxy,
- carboxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- Cl, Br,
- amino,
- amidino,
- guanidino,
- N,N'-di-(benzyloxycarbonyl)-guanidino,
- Carbamoyl,
- (C<sub>7</sub>-C<sub>15</sub>)-aralkoxycarbonyl,
- (C<sub>1</sub>-C<sub>5</sub>)-alkoxycarbonylamino,
- (C<sub>7</sub>-C<sub>15</sub>)-aralkoxycarbonylamino or
- 9-fluorenylmethoxycarbonylamino;
- (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl, the aryl part in each case possibly being substituted by one, two or three identical or different radicals from the series
- F, Cl, Br, I,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- amino and
- trifluoromethyl; or

- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, het standing for the radical of a 5- or 6-member monocyclic or 9- to 10-member bicyclic, possibly partly or completely hydrogenated heteroaromatic compound with at least 1 C atom, 1-4 N atoms and/or 1-2 S atoms and/or 1-2 O atoms as ring members, which is possibly mono- or di-substituted as described in claim 1 for the aryl part; or  
b<sub>2</sub>) together with R<sup>4</sup> or R<sup>4\*</sup> and the atoms carrying these form pyrrolidine or piperidine, which in each case can also be annelated, with cyclopentyl, cyclohexyl or phenyl,  
or together with R<sup>3</sup> or R<sup>3\*</sup> and the atoms carrying these form cyclic, saturated or partly unsaturated ring systems with 3-8 ring members;

R<sup>3</sup> and R<sup>3\*</sup>

independent of each other mean

- hydrogen,
- methyl or
- ethyl;

R<sup>4</sup> and R<sup>4\*</sup>

independent of each other mean

- hydrogen,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>5</sup>, R<sup>5\*</sup> and R<sup>5\*\*</sup>

independent of each other are as defined in claim 1;

R<sup>6</sup>, R<sup>6\*</sup> and R<sup>6\*\*</sup>

independent of one another mean

- hydrogen,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>7</sup>

means

- hydrogen,
- hydroxy or
- C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>8</sup> and R<sup>8\*</sup>

independent of each other mean

- hydrogen,
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl or together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form pyrrolidine or piperidine, which in each case can additionally be annelated with cyclopentyl, cyclohexyl or phenyl;

R<sup>9</sup> and R<sup>9\*</sup>

independent of each other are defined like R<sup>2</sup> or R<sup>2\*</sup> under b<sub>1</sub>), or mean (C<sub>1</sub>-C<sub>8</sub>)-alkyl, or

together with R<sup>10</sup> or R<sup>10\*</sup> and the atoms carrying these form a mono- or bicyclic, saturated or partly unsaturated ring system with 5-12 ring members;

or

together with R<sup>11</sup> or R<sup>11\*</sup> and the atoms carrying these form a mono- or bicyclic, saturated or partly unsaturated ring system with 5-12 ring elements, which in addition to carbon can also contain 1 sulfur atom which can possibly be oxidized to sulfoxide or sulfone;

R<sup>10</sup> and R<sup>10\*</sup>

independent of each other mean

- hydrogen or
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>11</sup> and R<sup>11\*</sup>

independent of each other mean

- hydrogen,
- hydroxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy or
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>12</sup>, R<sup>12\*</sup>, R<sup>13</sup> and R<sup>13\*</sup>

independent of one another mean

- hydrogen,
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl, which can be substituted by
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- carboxy,
- hydroxy or
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>14</sub>)-alkoxycarbonyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl, which can be substituted as described for R<sup>1</sup> or R<sup>1\*</sup>,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- het or
- het-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, het being defined as described for R<sup>1</sup> or R<sup>1\*</sup>,

it being possible in the aforementioned compounds of formula I for one or more amide groups (-CONH-) of the main chain to be replaced by a group consisting of -CH<sub>2</sub>-NR<sup>14</sup>-, -CH<sub>2</sub>-O-, -CH<sub>2</sub>CH<sub>2</sub>-, -COCH<sub>2</sub>-, -CH(OH)CH<sub>2</sub>-, -COO- or by an amide group of reverse polarity (-NHCO-);

R<sup>14</sup> stands for

- hydrogen or
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

as well as their physiologically tolerated salts.

5. Compounds of formula I as described in claims 1 to 4, characterized in that

Y stands for a radical of formula II or a radical of formula III;

l, m, A, A\*, D, D\*, n, n\*, o, o\* are defined as in claim 1,

p and p\* stand for 1;

R<sup>1</sup> and R<sup>1\*</sup>

independent of each other stand for

- hydrogen,
- carboxyl,
- (C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- phenyl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl, which in the phenyl part can be substituted as in claim 4,
- possibly protected mono- or di-amino-(C<sub>1</sub>-C<sub>12</sub>)-alkyl or amino-(C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl or amino-(C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, such as -2-amino-3-phenyl-propyl,
- mono-, di-, tris-, tetra-, penta- or hexahydroxy-(C<sub>1</sub>-C<sub>10</sub>)-alkyl or -alkanoyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>16</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkylsulfinyl,
- mono-, di-, trihydroxy-(C<sub>1</sub>-C<sub>8</sub>)-alkylsulfonyl,
- mono-, di-, trihydroxy-(C<sub>1</sub>-C<sub>8</sub>)-alkylsulfinyl,
- mono-, di-, tri- or tetra-(C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,

- (C<sub>1</sub>-C<sub>14</sub>)-alkanoyl,
- possibly protected amino-(C<sub>1</sub>-C<sub>11</sub>)-alkanoyl,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino-(C<sub>2</sub>-C<sub>11</sub>)-alkanoyl,
- (C<sub>1</sub>-C<sub>9</sub>)-cycloalkylcarbonyl,
- amino-substituted (C<sub>3</sub>-C<sub>9</sub>)-cycloalkylcarbonyl,
- amino-substituted (C<sub>3</sub>-C<sub>9</sub>)-cycloalkylsulfonyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>2</sub>-C<sub>11</sub>)-alkanoyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryloxy-(C<sub>2</sub>-C<sub>11</sub>)-alkanoyl,
- benzoyl, benzenesulfonyl or (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkylcarbonyl or -sulfonyl  
possibly substituted by amino, halogen, (C<sub>1</sub>-C<sub>7</sub>)-alkyl, (C<sub>1</sub>-C<sub>7</sub>)-alkoxy or  
(C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- (C<sub>1</sub>-C<sub>10</sub>)-alkoxycarbonyl,
- substituted (C<sub>1</sub>-C<sub>10</sub>)-alkoxycarbonyl
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl, (C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl or (C<sub>1</sub>-C<sub>10</sub>)  
substituted by possibly protected amino and hydroxy,
- 9-flourenylmethoxycarbonyl,
- ketohexosyl,
- ketopentosyl,
- deoxyhexoketosyl,
- dexoypentoketosyl,
- aldohexosyl,
- aldopentosyl,
- deoxyhexoaldosyl,
- deoxypentoaldosyl,
- 2-amino-2-deoxyhexosyl

- 2-acetamido-2-deoxyhexosyl,
- lactosyl or
- maltosyl, it being possible for the joined sugar to be present in the pyranose or furanose form,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-carbonyl or -sulfonyl,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkylcarbonyl or -sulfonyl,
- het-mercapto-(C<sub>1</sub>-C<sub>6</sub>)-alkylcarbonyl or -sulfonyl,

het in each case standing for

furyl, thienyl, benzothienyl, benzodioxolanyl, pyrrolyl, imidazolyl, isoxazolyl, thiazolyl, pyrazolyl, triazolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazinyl, pyrrolidyl, piperidyl, piperazinyl, morpholino, thiomorpholino, tetrahydrofuryl, tetrahydropyryl, tetrahydrothienyl, indolyl, quinolyl or isoquinolyl,

it also being possible for these to be substituted by one or two identical or different radicals from the group (C<sub>1</sub>-C<sub>4</sub>)-alkyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxy, (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino, hydroxy, amino, mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino and oxido;

R<sup>2</sup> and R<sup>2\*</sup>

independent of each other mean

- hydrogen,
- carboxyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl, which is possibly substituted by up to 2 identical or different radicals from the series
- hydroxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,

- (C<sub>1</sub>-C<sub>4</sub>)-alkylthio,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfinyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy,
- carboxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- amino,
- amidino,
- guanidino,
- N,N'-di-(benzyloxycarbonyl)-guanidino,
- carbamoyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkoxycarbonyl,
- (C<sub>1</sub>-C<sub>5</sub>)-alkoxycarbonylamino,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkoxycarbonylamino, or
- (C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl-(C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl, the aryl part possibly being substituted by one, two or three identical or different radicals from the series
- F, Cl, Br,
- hydroxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl and
- amino, or

- het-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, het being defined as for R<sup>1</sup> or R<sup>1\*</sup>,

R<sup>3</sup> and R<sup>3\*</sup>

independent of each other mean

- hydrogen or

- methyl,

R<sup>4</sup> and R<sup>4\*</sup>

independent of each other mean

- hydrogen or

- methyl,

R<sup>5</sup>, R<sup>5\*</sup> and R<sup>5\*\*</sup>

independent of one another mean

- hydrogen,

- hydroxy,

- amino or

- carboxy;

R<sup>6</sup>, R<sup>6\*</sup> and R<sup>6\*\*</sup>

independent of one another mean

- hydrogen or

- methyl;

R<sup>7</sup> means

- hydrogen,

- hydroxy or

- methyl;

R<sup>8</sup> and R<sup>8\*</sup>

independent of each other mean

- hydrogen,

- methyl, ethyl or n-propyl, or together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form a 1,2,3,4-tetrahydroisoquinoline or a 2-azabicyclooctane skeleton;  
R<sup>9</sup> and R<sup>9\*</sup>

independent of each other are defined like R<sup>2</sup> and R<sup>2\*</sup> in claim 4, or mean  
(C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy or

together with R<sup>10</sup> or R<sup>10\*</sup> and the atoms carrying these form cyclic ring systems with 5 to 7 ring members;

or together with R<sup>11</sup> or R<sup>11\*</sup> form a thiochroman system the sulfur atom of which can if appropriate be oxidized to sulfone;

R<sup>10</sup> and R<sup>10\*</sup>

independent of each other mean

- hydrogen or

- methyl;

R<sup>11</sup> and R<sup>11\*</sup> are defined as in claim 4;

in the aforementioned compounds of formula I one or more amide groups (-CONH-) of the main chain can be replaced as defined in claim 4;

R<sup>14</sup> stands for

- hydrogen or

- methyl;

as well as their physiologically tolerated salts.

6. Compound of formula I as contained in claims 1 to 5, characterized in that

$R^1$  and  $R^{1*}$

independent of each other stand for

$a_1$ ) - hydrogen,

- carboxyl,

-  $(C_1-C_{16})$ -alkylsulfonyl

-  $(C_1-C_8)$ -alkylsulfinyl,

-  $(C_1-C_8)$ -mono-, di- or tri-hydroxyalkylsulfonyl,

- hydroxy- $(C_1-C_{10})$ -alkanoyl,

- mono-, di-, tri- or tetra-hydroxy- $(C_1-C_4)$ -alkyl,

-  $(C_1-C_8)$ -alkanoyloxy- $(C_1-C_{10})$  alkyl,

- 1,2-diacetoxyethyl,

- 1,2,3-triacetoxypropyl,

-  $(C_1-C_{14})$ -alkanoyl,

- amino- $(C_1-C_{12})$ -alkanoyl,

- N- $(C_1-C_4)$ -alkoxycarbonylamino- $(C_1-C_8)$ -alkyl,

- di- $(C_1-C_7)$ -alkylamino- $(C_2-C_{11})$ -alkanoyl,

-  $(C_3-C_9)$ -cycloalkylcarbonyl,

- amino- $(C_3-C_8)$ -cycloalkylcarbonyl,

- amino- $(C_3-C_8)$ -cycloalkylsulfonyl,

- phenyl,

-  $(C_6-C_{10})$ -aryl- $(C_2-C_{11})$ -alkanoyl,

-  $(C_6-C_{10})$ -aryloxy- $(C_2-C_{11})$ -alkanoyl,

- benzoyl or benzenesulfonyl, possibly substituted by halogen, amino,  $(C_1-C_7)$ -alkyl,  $(C_1-C_7)$ -alkoxy or  $(C_1-C_7)$ -alkoxycarbonyl,

- benzylsulfonyl, benzylsulfinyl or benzylthio, possibly substituted by halogen, amino, (C<sub>1</sub>-C<sub>7</sub>)-alkyl, (C<sub>1</sub>-C<sub>7</sub>)-alkoxy or (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- 4-chlorobenzylsulfonyl,
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,
- (C<sub>1</sub>-C<sub>12</sub>)-alkanoyl which is substituted by hydroxy, amino and possibly by phenyl or cyclohexyl,
- possibly protected, amino-substituted (C<sub>6</sub>-C<sub>10</sub>)-aryl- or (C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>1</sub>-C<sub>8</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>10</sub>)-alkoxycarbonyl,
- substituted (C<sub>1</sub>-C<sub>10</sub>)-alkoxycarbonyl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonyl,
- 9-fluorenylmethoxycarbonyl,
- 1-deoxyhexoketosyl or 1-deoxypentoketosyl,
- hexosyl or pentosyl
- 6-deoxyhexosyl,
- amino sugar radicals,
- lactosyl,
- maltosyl,

it being possible for the joined sugar to be present in the pyranose or furanose form,

- het,
- het-carbonyl or het-sulfonyl,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkanoyl
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkylsulfonyl or

- het-mercapto-(C<sub>1</sub>-C<sub>3</sub>)-alkylcarbonyl,

het standing in each case for

- pyrrolyl,

- imidazolyl,

- pyridyl,

- pyrimidyl,

- pyrrolidyl,

- piperidyl,

- morpholino,

- quinolyl or

- isoquinolyl,

and also possibly being substituted by one or two identical or different

radicals from the group (C<sub>1</sub>-C<sub>4</sub>)-alkyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl, (C<sub>1</sub>-C<sub>4</sub>)-

alkoxycarbonylamino, hydroxy, amino, mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino;

R<sup>2</sup> and R<sup>2\*</sup>

independent of each other stand for

- hydrogen,

- carboxyl,

- methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec.-butyl, n-pentyl,  
n-hexyl,

- cyclohexyl,

- cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl,

- 4-methylcyclohexylmethyl,

- 1-decahydronaphthylmethyl, 2-decahydronaphthylmethyl,

- phenyl,

- benzyl,

- 2-phenylethyl,
- 1-naphthylmethyl, 2-naphthylmethyl,
- 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl,
- 2,4,6-trimethylbenzyl,
- 4-tert.-butylbenzyl,
- 4-tert.-butoxybenzyl
- 4-hydroxybenzyl,
- 4-methoxybenzyl,
- 2,4-dimethoxybenzyl,
- 3,4-dihydroxybenzyl,
- 3,4-dimethoxybenzyl,
- (benzodioxolane-5-yl)methyl,
- 4-chlorobenzyl,
- hydroxymethyl,
- 1-hydroxyethyl,
- 4-pyridyl,- 4-(N-oxidopyridyl),
- 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, 2-(4-pyridyl)-ethyl,
- 2-thienylmethyl, 3-thienylmethyl,
- 2-(2-thienyl)ethyl, 2-(3-thienyl)ethyl,
- indole-2-yl-methyl, indole-3-yl-methyl,
- (1-methyl-imidazole-4-yl)methyl,
- imidazole-4-yl-methyl, imidazole-1-yl-methyl,
- 2-thiazolylmethyl,
- 3-pyrazolylmethyl,
- 4-pyrimidylmethyl,
- 2-benzo[b]thienylmethyl, 3-benzo[b]thienylmethyl,

- 2-furylmethyl,
- 2-(methylthio)ethyl,
- 2-(methylsulfinyl)ethyl

$R^3$ ,  $R^{3*}$ ,  $R^4$ ,  $R^{4*}$ ,  $R^6$ ,  $R^{6*}$ ,  $R^{10}$  and  $R^{10*}$

mean hydrogen;

$R^5$  and  $R^{5*}$

independent of each other stand for

- hydrogen,
- hydroxy or
- amino;

$R^7$  means

- hydroxy or
- methyl;

$R^8$  and  $R^{8*}$

independent of each other mean

- hydrogen or

together with  $R^9$  or  $R^{9*}$  and the atoms carrying these form a 1,2,3,4-tetrahydroisoquinoline or 2-azabicyclooctane skeleton;

$R^9$  and  $R^{9*}$

independent of each other are defined like  $R^2$  or  $R^{2*}$  or mean

- hydroxy,
- acetoxy,
- tert.-butoxymethyl,
- 3-guanidinopropyl,
- carbamoylmethyl, carbamoylethyl,
- carboxymethyl, carboxyethyl,

- mercaptomethyl,
- (1-mercapto-1-methyl)ethyl,
- aminomethyl, 2-aminoethyl, 3-aminopropyl, 4-aminobutyl,
- N,N-dimethylamino,
- N,N'-di-(benzyloxycarbonyl)-guanidino-propyl,
- 2-benzyloxycarbonyl ethyl, benzyloxycarbonylmethyl,
- tert.-butylsulfonylmethyl
- 4-benzylcarbonylaminobutyl;

$R^{11}$  and  $R^{11*}$

independent of each other mean

- hydrogen,
- hydroxy or
- acetoxy,

and in the aforementioned compounds of this invention one or more amide groups (-CONH-) of the main chain can be replaced by  $-CH_2NR^{14}-$  or  $-CH(OH)CH_2-$ ;

$R^{14}$  stands for

- hydrogen or
- methyl;

as well as their physiologically tolerated salts.

7. Compound of formula I as contained in claims 1 to 6, characterized in that

$R^1$  and  $R^{1*}$

independent of each other stand for

- a<sub>1</sub>) - hydrogen,
- carboxyl,
- (C<sub>1</sub>-C<sub>16</sub>)-alkylsulfonyl,

- (C<sub>1</sub>-C<sub>8</sub>)-mono- or -dihydroxyalkylsulfonyl,
  - mono-, di- or trihydroxy-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
  - (C<sub>1</sub>-C<sub>8</sub>)-alkoxycarbonyl,
  - (C<sub>1</sub>-C<sub>14</sub>)-alkanoyl,
  - amino-(C<sub>1</sub>-C<sub>12</sub>)-alkanoyl,
  - (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
  - (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkylcarbonyl,
  - 9-fluorenylmethoxycarbonyl,
  - (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
  - 1,2-diacetoxyethyl,
  - 1,2,3-triacetoxypropyl,
  - phenyl
  - benzolsulfonyl possibly substituted by halogen, amino, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or methoxy,
  - benzolsulfonyl, -sulfinyl or -thio possibly substituted by halogen, amino, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or methoxy,
  - het or het-sulfonyl,
  - het-(C<sub>1</sub>-C<sub>4</sub>)-alkanoyl,
  - het-mercapto-(C<sub>1</sub>-C<sub>3</sub>)-alkylcarbonyl,
- het in each case standing for
- pyrrolyl,
  - imidazolyl,
  - pyridyl,
  - pyrimidyl,
  - pyrrolidyl,
  - quinolyl,

- isoquinolyl,
- piperidyl or
- morpholino,

it also being possible that this radical is substituted by one or two identical or different radicals from the group methyl, amino and (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,

- amino-(C<sub>3</sub>-C<sub>6</sub>)-cycloalkylcarbonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkanoyl, which is substituted by hydroxy and amino and possibly by phenyl or cyclohexyl,
- possibly protected amino-substituted phenyl- or cyclohexyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,
- benzyloxycarbonylamino,
- 1-deoxyhexoketosyl or 1-deoxypentoketosyl,
- hexosyl or pentosyl, it being possible for the joined sugar to be present in the pyranose or the furanose form,

R<sup>2</sup> and R<sup>2\*</sup>

independent of each other stand for

- hydrogen,
- methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec.-butyl, pentyl, hexyl,
- cyclopentylmethyl, cyclohexylmethyl,
- 4-methylcyclohexylmethyl,
- benzyl,
- 2-phenylethyl,
- 1-naphthylmethyl, 2-naphthylmethyl,

- 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl,
- 2,4,6-trimethylbenzyl,
- 4-tert.-butylbenzyl,
- 4-methoxybenzyl,
- 3,4-dihydroxybenzyl,
- 2,4-dimethoxybenzyl,
- 3,4-dimethoxybenzyl,
- 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl or
- 3,4-dimethylenedioxybenzyl,
- 2-(4-pyridyl)ethyl;

$R^3$ ,  $R^{3*}$ ,  $R^4$ ,  $R^{4*}$ ,  $R^6$ ,  $R^{6*}$ ,  $R^7$ ,  $R^{10}$  AND  $R^{10*}$

mean hydrogen;

$R^5$  and  $R^{5*}$

independent of each other mean

- hydrogen or
- hydroxy;

$R^8$  and  $R^{8*}$  independent of each other are defined as in claim 6,

$R^9$  and  $R^{9*}$

independent of each other are defined like  $R^9$  and  $R^{9*}$  in claim 6;

$R^{11}$  and  $R^{11*}$  independent of each other are defined as in claim 6,

as well as their physiologically tolerated salts.

8. Compound of formula I as contained in claims 1 to 7, characterized in that

Y stands for a radical of formula III;

l means 0 or 1;

m means 1;

A, A\*, D and D\* are defined as in claim 1;

n, n\*, o, o\*, p and p\* independent of one another mean 1;

E, E\*, F, F\*, G and G\* independent of one another stand for an amino acid from the series Val, Lys, Lys(Z), Phe, Chg, Ser, Asn, Gly, Ile, Tbg, Nva or Npg;

R<sup>1</sup> and R<sup>1\*</sup> independent of each other mean

- hydrogen,
- carboxyl,
- methylsulfonyl,
- tert.-butylsulfonyl,
- tert.-butoxycarbonyl,
- 2-hydroxyethylsulfonyl,
- 1,2,3-trihydroxypropyl,
- 1,2,3-triacetoxypropyl,
- benzyloxycarbonyl,
- 4-methylphenylsulfonyl,
- 4-chlorobenzylthio,
- benzylsulfinyl,
- 4-chlorobenzylsulfonyl,
- hexadecylsulfonyl,
- 4-amino-1-piperidyl-sulfonyl,
- N-tert.-butoxycarbonyl-4-amino-1-piperidyl-sulfonyl,
- 4-amino-1-piperidyl-carbonyl,
- N-tert.-butoxycarbonyl-4-amino-1-piperidyl-carbonyl,
- 2-amino-3-phenyl-propyl,
- N-tert.-butoxycarbonyl-2-amino-3-phenyl-propyl,
- 2-amino-1-hydroxy-4-methyl-pentyl,

- deoxyfructos-1-yl,
- mannofuranosyl,
- 4-aminocyclohexylcarbonyl,
- 2-quinolylcarbonyl,
- 4-pyridylthio-acetyl,
- 2-quinolyl carbonyl,
- 1-naphthylacetyl,
- 1-naphthyloxyacetyl,
- 1-(4-pyridyl)-ethylsulfonyl,
- 12-aminododecanoyl,
- 4-(N-oxidopyridyl),
- 4-pyridyl,
- tetradecanoyl,
- phenyl,
- amino or
- tert.-butoxycarbonylamino;

$R^2$  and  $R^{2*}$  independent of each other mean

- hydrogen,
- 2-(4-pyridyl)ethyl,
- isopropyl,
- isobutyl,
- n-pentyl,
- benzyl,
- 3,4-methylenedioxybenzyl,
- 2,4-dimethoxybenzyl,
- 4-tert.-butylbenzyl,

- 2-phenylethyl or

- cyclohexylmethyl;

$R^3$ ,  $R^{3*}$ ,  $R^4$ ,  $R^{4*}$ ,  $R^6$ ,  $R^{6*}$ ,  $R^7$ ,  $R^{10}$  and  $R^{10*}$  mean

- hydrogen;

$R^5$  and  $R^{5*}$  independent of each other mean

- hydrogen or

- hydroxy;

$R^8$  and  $R^{8*}$  mean

- hydrogen, or together with  $R^9$  or  $R^{9*}$  and the atoms carrying these form a 1,2,3,4-tetrahydroquinoline-3,4-diyl system;

$R^9$  and  $R^{9*}$  independent of each other mean

- hydrogen,

- hydroxy,

- acetoxy,

- n-propyl,

- isopropyl,

- isobutyl,

- aminomethyl,

- 4-aminobutyl,

- hydroxymethyl,

- tert.-butoxymethyl,

- aminocarbonylmethyl,

- 2-benzyloxycarbonyl-ethyl,

- 4-benzylcarbonylamino-butyl,

- N,N'-di(benzyloxycarbonyl)-guanidino-propyl,

- cyclohexyl,

- cyclohexylmethyl,
- benzyl,
- 2-phenyl-ethyl,
- 4-hydroxy-benzyl,
- 4-methoxy-benzyl,
- 4-tert.-butoxy-benzyl,
- 1-naphthylmethyl,
- 2-thienylmethyl,
- 1-imidazolyl-methyl,
- 3-indolyl-methyl,
- 4-pyridylmethyl,
- 4-(N-oxidopyridyl)methyl,
- 2-methylthio-ethyl,
- 2-methylsulfonyl-ethyl,
- tert.-butylsulfonyl-methyl or
- 2-carboxyl-ethyl;

R<sup>11</sup> and R<sup>11\*</sup> independent of each other mean

- hydrogen
- hydroxy or
- acetoxy;

it being possible in the aforementioned compounds that one or more amide groups (-CONH-) of the main chain are replaced by -CH<sub>2</sub>NH- or -CH(OH)CH<sub>2</sub>-; as well as their physiologically tolerated salts.

9. Compound of formula I as contained in claims 1 to 8, characterized in that

l = 0;

$m = 1;$

$n + o + p = 1;$

D and D\* stand for a radical of formula VI or VI\*;

R<sup>1</sup> and R<sup>1\*</sup> mean

- (C<sub>1</sub>-C<sub>12</sub>)-alkylsulfonyl, which can possibly be substituted by up to 3 identical or different radicals from the series

- hydroxy,

- amino or

- carboxy;

R<sup>2</sup> and R<sup>2\*</sup> independent of each other mean

- hydrogen,

- carboxyl,

- methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec.-butyl, pentyl, hexyl,

- cyclohexyl,

- cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl,

- 4-methylcyclohexylmethyl,

- 1-decahydronaphthylmethyl, 2-decahydroanaphthylmethyl,

- phenyl,

- benzyl,

- 2-phenylethyl,

- 1-naphthylmethyl, 2-naphthylmethyl,

- 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl,

- 2,4,6-trimethylenzyl,

- 4-tert.-butylbenzyl,

- 4-tert.-butoxybenzyl,

- 4-hydroxybenzyl,
- 4-methoxybenzyl,
- 2,4-dimethoxybenzyl,
- 3,4-dihydroxybenzyl,
- 3,4-dimethoxybenzyl,
- (benzodioxolane-4-yl)methyl,
- 4-chlorobenzyl,
- hydroxymethyl,
- 1-hydroxyethyl,
- 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, 2-(4-pyridyl)-ethyl,
- 2-thienylmethyl, 3-thienylmethyl,
- 2-(2-thienyl)ethyl, 2-(3-thienyl)ethyl,
- indole-2-yl-methyl, indole-3-yl-methyl,
- (1-methyl-imidazole-4-yl)methyl,
- imidazol-4-yl-methyl, imidazol-1-yl-methyl,
- 2-thiazolylmethyl,
- 3-pyrazolylmethyl,
- 4-pyrimidylmethyl,
- 2-benzo[b]thienylmethyl, 3-benzo[b]thienylmethyl,
- 2-furylmethyl,
- 2-(methylthio)ethyl,
- 2-(methylsulfinyl)ethyl or
- 2-(methylsulfonyl)ethyl;

R<sup>3</sup>, R<sup>3\*</sup>, R<sup>4</sup>, R<sup>4\*</sup>, R<sup>6</sup>, R<sup>6\*</sup>, R<sup>11</sup> and R<sup>11\*</sup> mean

- hydrogen;

R<sup>5</sup> and R<sup>5\*</sup> mean

- hydroxy;

R<sup>9</sup> and R<sup>9\*</sup>

are defined as in claim 8;

as well as their physiologically tolerated salts.

10. Process for the production of a compound of formula I as contained in claims 1 to 9, characterized in that a fragment with terminal carboxyl group or its reactive derivative is coupled to a corresponding fragment with free amino group, possibly for the protection of other functional groups (a) temporarily introduced protective group(s) is split off, and the compound thus obtained is, if appropriate, converted into its physiologically tolerated salt.

11. Use of a compound of formula I as contained in claims 1 to 9 as a drug.

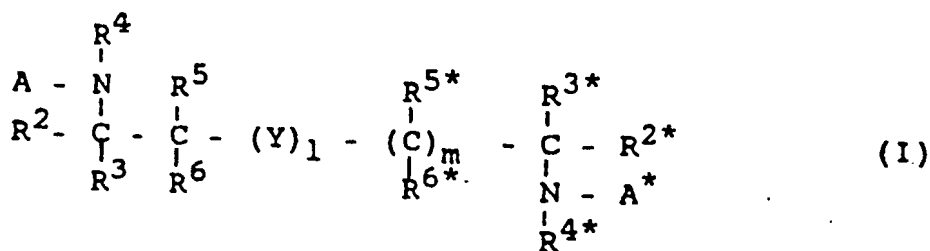
12. Use of a compound of formula I as contained in claims 1 to 9 for inhibiting retroviral proteases.

13. Use of a compound of formula I as contained in claims 1 to 9 in the treatment of "acquired immune deficiency syndrome."

14. Pharmaceutical agent containing a compound of formula I as contained in claims 1 to 9 as well as one or more carriers, if appropriate.

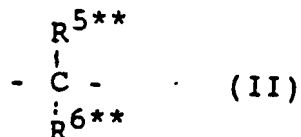
Patent claims for the following treaty countries: ES, GR

1. Process for the production of a compound of formula I



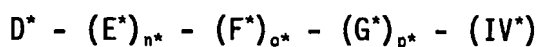
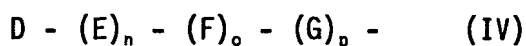
wherein

Y stands for oxygen, sulfur, a radical of formula II or a radical of formula III



l and m, independent of each other, are 0 or 1;

A means a radical of formula IV and A\* a radical of formula IV\*



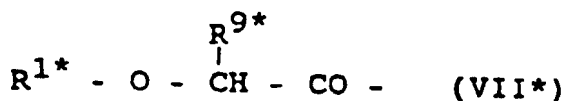
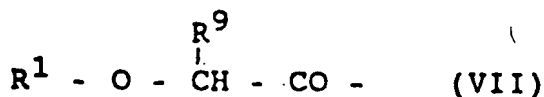
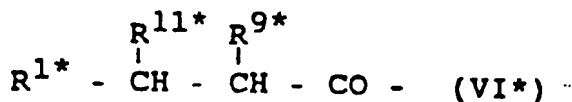
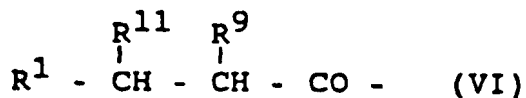
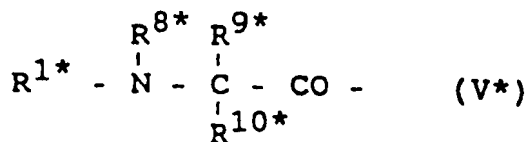
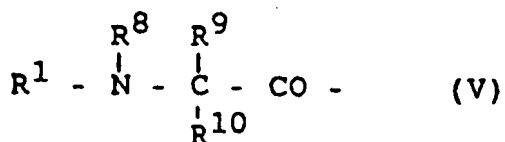
where

E, E\*, F, F\*, G and G\*, independent of one another, stand for a natural or an unnatural amino acid, azaamino acid or imino acid;

n, n\*, o, o\*, p and p\*, independent of one another, mean 0 or 1;

D stands for R<sup>1</sup> or a radical of formulas V, VI or VII, and

D\* stands for R<sup>1\*</sup> or a radical of formulas V\*, VI\* or VII\*



and wherein R<sup>1</sup> and R<sup>1\*</sup>, independent of each other, stand for

a<sub>1</sub>)

- hydrogen
- carboxyl.
- (C<sub>1</sub>-C<sub>18</sub>)-alkyl, which may be simply or doubly unsaturated and which may be substituted by up to 3 identical or different radicals from the series
- mercapto,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- carbamoyl
- (C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy,
- carboxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- F, Cl, Br, I,
- amino
- amidino, which if appropriate can be substituted by one, two or three (C<sub>1</sub>-C<sub>8</sub>)-alkyl radicals,
- guanidino, which if appropriate can be substituted by one or two benzyloxycarbonyl radicals or by one, two, three or four (C<sub>1</sub>-C<sub>8</sub>)-alkyl radicals,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino,
- (C<sub>7</sub>-C<sub>15</sub>)-aralkoxycarbonyl,
- (C<sub>7</sub>-C<sub>15</sub>)-aralkoxycarbonylamino,
- phenyl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxy
- 9-fluorenylmethoxycarbonylamino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylsulfonyl,

- (C<sub>1</sub>-C<sub>6</sub>)-alkylsulfinyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkylthio,
- hydroxamino,
- hydroximino,
- sulfamoyl,
- sulfo,
- carboxamido,
- formyl,
- hydrazono,
- imino,
- a radical CONR<sup>12</sup>R<sup>13</sup> or CONR<sup>12\*</sup>R<sup>13\*</sup>,
- by up to six hydroxy or
- by up to five (C<sub>1</sub>-C<sub>6</sub>)-alkanoxyloxy;
- mono-, bi- or tri-cyclic (C<sub>3</sub>-C<sub>18</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>18</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, the cycloalkyl part in each case being substituted if appropriate by one or two identical or different radicals from the series
- F, Cl, Br, I,
- carboxy,
- carbamoyl,
- carboxymethoxy,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyloxycarbonyl,
- amino,

- (C<sub>1</sub>-C<sub>6</sub>)-alkylamino-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- di-(C<sub>1</sub>-C<sub>6</sub>)-alkylamino-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- amidino,
- hydroxamino,
- hydroximino,
- hydrazono,
- imino,
- guanidino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxysulfonyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxysulfinyl,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino
- (C<sub>6</sub>-C<sub>12</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino and
- trifluoromethyl;
- (C<sub>6</sub>-C<sub>14</sub>)-aryl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryloxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl or
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl, wherein the aryl part in each case is substituted if appropriate by one, two or three identical or different radicals from the series
- F, Cl, Br, I,
- hydroxy,
- mono-, di- or tri-hydroxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- trifluoromethyl,
- formyl,

- carboxamido,
- mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylaminocarbonyl,
- nitro,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- carboxy,
- carboxymethoxy,
- amino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino-(C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonylmethoxy,
- carbamoyl,
- sulfamoyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxysulfonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkylsulfonyl,
- sulfo-(C<sub>1</sub>-C<sub>8</sub>)-alkyl
- guanidino (C<sub>1</sub>-C<sub>8</sub>)-alkyl and
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino;
- het,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,
- het-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,

- het-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkoxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- het-thio-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-thio-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,
- het-thio-(C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,

where in each case het stands for the radical of a 5- to 7-member monocyclic or 8- to 10-member bicyclic ring system which can be benzannellated, aromatic, partly hydrogenated or completely hydrogenated, which can contain as heteroelements one, two, three or four different radicals from the group N, O, S, NO, SO, SO<sub>2</sub>, which can be substituted with 1 to 6 hydroxy and which, if appropriate, is mono-, di- or tri-substituted as defined for (C<sub>6</sub>-C<sub>14</sub>)-aryl under a<sub>1</sub>) and/or with oxo,

or mean a radical NR<sup>12</sup>R<sup>13</sup> or NR<sup>12\*</sup>R<sup>13\*</sup>,

or

a<sub>2</sub>)

- a radical of formula VIII or VIII\*

R<sup>1a</sup>-W (VIII)

R<sup>1a\*</sup>-W\* (VIII\*)

wherein R<sup>1a</sup> and R<sup>1a\*</sup> are defined like R<sup>1</sup> and R<sup>1\*</sup> under a<sub>1</sub>) and W and W\* stand for -CO-, -CS-, O-CO-, -SO<sub>2</sub>-, -SO-, -S-, -NHSO<sub>2</sub>-, -NHCO-, -CH(OH)-, -N(OH)- or -CO-V- with V meaning a peptide with 1 to 10 amino acids;

or wherein R<sup>1</sup> and R<sup>1\*</sup>, independent of each other, together with R<sup>11</sup> or R<sup>12</sup> and the atoms that carry them form monocyclic or bicyclic, saturated or partly unsaturated ring systems with 5-12 ring members which in addition to carbon can also contain 1 sulfur atom, which may be oxidized to sulfoxide or sulfone;

a<sub>3</sub>)

- a glycosyl radical, preferably a glucofuranosyl or glucopyranosyl radical, which is derived from naturally occurring aldotetroses, aldopentoses, aldohexoses, ketopentoses, ketohexoses, desoxyaldoses, aminoaldoses and oligosaccharides as well as their stereoisomers;

R<sup>2</sup> and R<sup>2\*</sup>

are defined independent of each other like R<sup>1</sup> and R<sup>1\*</sup> under a<sub>1</sub>) or a<sub>2</sub>) or together with R<sup>4</sup> or R<sup>4\*</sup> and the atoms carrying them form mono- or bicyclic, saturated or partly unsaturated ring systems with 5 to 12 ring members, or together with R<sup>3</sup> or R<sup>3\*</sup> and the atoms carrying them form cyclic, saturated or partly unsaturated ring systems with 3 to 12 ring members;

R<sup>3</sup> and R<sup>3\*</sup>

independent of each other mean

- hydrogen or
- (C<sub>1</sub>-C<sub>3</sub>)-alkyl;

R<sup>4</sup> and R<sup>4\*</sup>,

independent of each other, mean

- hydrogen or
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl;

R<sup>5</sup>, R<sup>5\*</sup> and R<sup>5\*\*</sup>,

independent of one another, mean

- hydrogen.
- hydroxy,
- amino or
- carboxy, or

with  $R^6$ ,  $R^{6*}$  or  $R^{6**}$  together with the carbon atoms carrying these, in each case independent of one another, form a keto group;

$R^6$ ,  $R^{6*}$  and  $R^{6**}$ ,

independent of one another, mean

- hydrogen or
- $(C_1-C_6)$ -alkyl or

in the case of  $l=0$ ,  $R^6$  and  $R^{6*}$  can possibly form a common bond;

$R^7$  means

- hydrogen,
- hydroxy or
- $(C_1-C_6)$ -alkyl;

$R^8$  and  $R^{8*}$ ,

independent of each other, mean

- hydrogen or
- $(C_1-C_6)$ -alkyl, or together with  $R^9$  or  $R^{9*}$  and the atoms carrying these form mono- or bicyclic, saturated or partly unsaturated ring systems with 5 to 12 ring members;

$R^9$  and  $R^{9*}$

independent of each other are defined like  $R^1$  or  $R^{1*}$  under  $a_1$ ), stand for hydroxy or  $(C_1-C_4)$ -alkanoyloxy, or together with  $R^{10}$  or  $R^{10*}$  and the atoms carrying these form cyclic, saturated or partly unsaturated ring systems with 3 to 12 ring members;

or

together with  $R^{11}$  or  $R^{11*}$  and the atoms carrying these form a mono- or bicyclic, saturated or partly unsaturated ring system with 5-12 ring members, which in addition to carbon can also contain 1 sulfur atom, which possibly can be

oxidized to sulfoxide or sulfone; or can contain 1 nitrogen atom, the ring system possibly being substituted by amino;

$R^{10}$  and  $R^{10*}$ ,

independent of each other, mean

- hydrogen or
- $(C_1-C_6)$ -alkyl;

$R^{11}$  and  $R^{11*}$ ,

independent of each other, mean

- hydrogen,
- hydroxy,
- $(C_1-C_4)$ -alkanoyloxy or
- $(C_1-C_8)$ -alkyl;

$R^{12}$ ,  $R^{12*}$ ,  $R^{13}$  and  $R^{13*}$ ,

independent of one another, mean

- hydrogen,
- $(C_1-C_8)$ -alkyl which can be substituted by
- amino,
- $(C_1-C_4)$ -alkylamino,
- di- $(C_1-C_4)$ -alkylamino,
- mercapto,
- carboxy,
- hydroxy or
- $(C_1-C_4)$ -alkoxy,
- $(C_3-C_7)$ -cycloalkyl,
- $(C_1-C_4)$ -alkoxycarbonyl,

- (C<sub>6</sub>-C<sub>14</sub>)-aryl, - (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl which in the aryl part can be substituted as described for R<sup>1</sup> or R<sup>1\*</sup>,

- het or

- het-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, het being defined as described for R<sup>1</sup> or R<sup>1\*</sup>,

or where R<sup>12</sup> and R<sup>13</sup> or R<sup>12\*</sup> and R<sup>13\*</sup> together with the nitrogen atoms carrying these form monocyclic or bicyclic, saturated, partly unsaturated or aromatic ring systems which in addition to carbon can also contain 1 or 2 nitrogen atoms, 1 sulfur atom or 1 oxygen atom as further ring members and which can be substituted by

(C<sub>1</sub>-C<sub>4</sub>)-alkyl,

where

in the compounds of formula I cited above, one or more amide groups (-CONH-) of the main chain can be replaced by -CH<sub>2</sub>NR<sup>14</sup>-, -CH<sub>2</sub>S-, -CH<sub>2</sub>O-, -OCH<sub>2</sub>-, CH<sub>2</sub>CH<sub>2</sub>-, -CH=CH-(cis and trans), -COCH<sub>2</sub>-, -CH(OH)CH<sub>2</sub>-, -CH<sub>2</sub>SO-, CH<sub>2</sub>SO<sub>2</sub>-, -COO-, P(O)(OR<sup>15</sup>)CH<sub>2</sub>- and -P(O)(OR<sup>15</sup>)NH-, or also by an amide group with reversed polarity (-HCHO-);

wherein R<sup>14</sup> and R<sup>15</sup>,

independent of each other, stand for

- hydrogen or

- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

as well as their physiologically tolerated salts, characterized in that a fragment with terminal carboxyl group or its reactive derivative is coupled with a corresponding fragment with free amino group, possibly (a) temporarily introduced protective group(s) for the protection of other functional groups is split off, and the compound thus obtained is converted, if appropriate, into its physiologically tolerated salt.

2. Process for the production of a compound of formula I as contained in claim 1, characterized in that the radicals and symbols with and without asterisk are identical in each case.

3. Process for the production of a compound of formula I as contained in claims 1 and 2, characterized in that the compound is  $C_2$ -symmetrical.

4. Process for the production of a compound of formula I as contained in claims 1 to 3, characterized in that Y stands for a radical of formula II or a radical of formula III;

l, m, A, A\*, D, D\*, n, n\*, o, o\*, p and p\* are defined as in claim 1;

E, E\*, F, F\*, G and G\*, independent of each other, stand for a natural or unnatural  $\alpha$ -amino acid or  $\alpha$ -imino acid;

R<sup>1</sup> and R<sup>1\*</sup>,

independent of each other, stand for

a<sub>1</sub>) - hydrogen,

- carboxyl,

- (C<sub>1</sub>-C<sub>16</sub>)-alkyl, which may be simply saturated and which may be substituted by up to 2 identical or different radicals from the series

- hydroxy,

- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,

- carbamoyl,

- (C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy,

- carboxy,

- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,

- F,

- amino,

- (C<sub>1</sub>-C<sub>7</sub>)-alkylamino,

- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino,
- benzyloxycarbonyl,
- benzyloxycarbonylamino,
- 9-fluorenylmethoxycarbonylamino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfonyl,
- a radical CONR<sup>12</sup>R<sup>13</sup> or CONR<sup>12\*</sup>R<sup>13\*</sup>,
- by up to six hydroxy or
- by up to four (C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy;
- mono- or bicyclic (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl where in each case the cycloalkyl part is substituted by one or two identical or different radicals from the series
- F,
- carboxy,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyloxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonylamino,
- benzyloxycarbonylamino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino and
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino;
- (C<sub>6</sub>-C<sub>10</sub>)-aryl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryloxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl or

- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, wherein the alkyl part in each case is possibly substituted by one, two or three identical or different radicals from the series
- F, Cl, Br,
- hydroxy,
- hydroxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- carboxamido,
- mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylaminocarbonyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- carboxy,
- carbamoyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino;
- het,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-(C<sub>5</sub>-C<sub>6</sub>)-cycloalkyl,
- het-thio-(C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- het-thio-(C<sub>5</sub>-C<sub>6</sub>)-cycloalkyl,

where het in each case stands for a 5- to 6-member monocyclic or 8- to 10-member bicyclic ring system which can be aromatic, partly hydrogenated or completely hydrogenated, which can contain as heteroelements one, two, three or four different radicals from the group N, O, S, NO, SO, SO<sub>2</sub>, which can be



- carboxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- Cl, Br,
- amino,
- amidino,
- guanidino,
- N,N'-di-(benzyloxycarbonyl)-guanidino,
- Carbamoyl,
- (C<sub>7</sub>-C<sub>15</sub>)-aralkoxycarbonyl,
- (C<sub>1</sub>-C<sub>5</sub>)-alkoxycarbonylamino,
- (C<sub>7</sub>-C<sub>15</sub>)-aralkoxycarbonylamino or
- 9-fluorenylmethoxycarbonylamino;
- (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>12</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl,
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl, the aryl part in each case possibly being substituted by one, two or three identical or different radicals from the series
- F, Cl, Br, I,
- hydroxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>7</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- amino and
- trifluoromethyl; or

- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, het standing for the radical of a 5- or 6-member monocyclic or 9- to 10-member bicyclic, possibly partly or completely hydrogenated heteroaromatic compound with at least 1 C atom, 1-4 N atoms and/or 1-2 S atoms and/or 1-2 O atoms as ring members, which is possibly mono- or di-substituted as described in claim 1 for the aryl part; or

b<sub>2</sub>) together with R<sup>4</sup> or R<sup>4\*</sup> and the atoms carrying these form pyrrolidine or piperidine, which in each case can also be annelated, with cyclopentyl, cyclohexyl or phenyl,

or together with R<sup>3</sup> or R<sup>3\*</sup> and the atoms carrying these form cyclic, saturated or partly unsaturated ring systems with 3-8 ring members;

R<sup>3</sup> and R<sup>3\*</sup>

independent of each other mean

- hydrogen,
- methyl or
- ethyl;

R<sup>4</sup> and R<sup>4\*</sup>

independent of each other mean

- hydrogen,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>5</sup>, R<sup>5\*</sup> and R<sup>5\*\*</sup>

independent of each other are as defined in claim 1;

R<sup>6</sup>, R<sup>6\*</sup> and R<sup>6\*\*</sup>

independent of one another mean

- hydrogen,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>7</sup>

means

- hydrogen,
- hydroxy or
- C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>8</sup> and R<sup>8\*</sup>

independent of each other mean

- hydrogen,
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl or together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form pyrrolidine or piperidine, which in each case can additionally be annelated with cyclopentyl, cyclohexyl or phenyl;

R<sup>9</sup> and R<sup>9\*</sup>

independent of each other are defined like R<sup>2</sup> or R<sup>2\*</sup> under b<sub>1</sub>), or mean (C<sub>1</sub>-C<sub>8</sub>)-alkyl, or

together with R<sup>10</sup> or R<sup>10\*</sup> and the atoms carrying these form a mono- or bicyclic, saturated or partly unsaturated ring system with 5-12 ring members;

or

together with R<sup>11</sup> or R<sup>11\*</sup> and the atoms carrying these form a mono- or bicyclic, saturated or partly unsaturated ring system with 5-12 ring elements, which in addition to carbon can also contain 1 sulfur atom which can possibly be oxidized to sulfoxide or sulfone;

R<sup>10</sup> and R<sup>10\*</sup>

independent of each other mean

- hydrogen or
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>11</sup> and R<sup>11\*</sup>

independent of each other mean

- hydrogen,
- hydroxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy or
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

R<sup>12</sup>, R<sup>12\*</sup>, R<sup>13</sup> and R<sup>13\*</sup>

independent of one another mean

- hydrogen,
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl, which can be substituted by
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino,
- carboxy,
- hydroxy or
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl, which can be substituted as described for R<sup>1</sup> or R<sup>1\*</sup>,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- het or
- het-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, het being defined as described for R<sup>1</sup> or R<sup>1\*</sup>,

it being possible in the aforementioned compounds of formula I for one or more amide groups (-CONH-) of the main chain to be replaced by a group consisting of -CH<sub>2</sub>-NR<sup>14</sup>-, -CH<sub>2</sub>O-, -OCH<sub>2</sub>-, CH<sub>2</sub>CH<sub>2</sub>-, -COCH<sub>2</sub>-, -CH(OH)CH<sub>2</sub>-, -COO- or by an amide group of reverse polarity (-NHCO-);

R<sup>14</sup> stands for

- hydrogen or
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl;

as well as their physiologically tolerated salts.

5. Process for the production of a compound of formula I as described in claims 1 to 4, characterized in that

Y stands for a radical of formula II or a radical of formula III;

l, m, A, A\*, D, D\*, n, n\*, o, o\* are defined as in claim 1, p and p\* stand for 1;

R<sup>1</sup> and R<sup>1\*</sup>

independent of each other stand for

- hydrogen,
- carboxyl,
- (C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- phenyl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl, which in the phenyl part can be substituted as in claim 4,
- possibly protected mono- or di-amino-(C<sub>1</sub>-C<sub>12</sub>)-alkyl or amino-(C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl or amino-(C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, such as -2-amino-3-phenyl-propyl,
- mono-, di-, tris-, tetra-, penta- or hexahydroxy-(C<sub>1</sub>-C<sub>10</sub>)-alkyl or -alkanoyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>16</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkylsulfinyl,
- mono-, di-, trihydroxy-(C<sub>1</sub>-C<sub>8</sub>)-alkylsulfonyl,
- mono-, di-, trihydroxy-(C<sub>1</sub>-C<sub>8</sub>)-alkylsulfinyl,
- mono-, di-, tri- or tetra-(C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy-(C<sub>1</sub>-C<sub>10</sub>)-alkyl,

- (C<sub>1</sub>-C<sub>14</sub>)-alkanoyl,
- possibly protected amino-(C<sub>1</sub>-C<sub>11</sub>)-alkanoyl,
- di-(C<sub>1</sub>-C<sub>7</sub>)-alkylamino-(C<sub>2</sub>-C<sub>11</sub>)-alkanoyl,
- (C<sub>1</sub>-C<sub>9</sub>)-cycloalkylcarbonyl,
- amino-substituted (C<sub>3</sub>-C<sub>9</sub>)-cycloalkylcarbonyl,
- amino-substituted (C<sub>3</sub>-C<sub>9</sub>)-cycloalkylsulfonyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>2</sub>-C<sub>11</sub>)-alkanoyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryloxy-(C<sub>2</sub>-C<sub>11</sub>)-alkanoyl,
- benzoyl, benzenesulfonyl or (C<sub>6</sub>-C<sub>19</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkylcarbonyl  
or -sulfonyl possibly substituted by amino, halogen, (C<sub>1</sub>-C<sub>7</sub>)-alkyl, (C<sub>1</sub>-C<sub>7</sub>)-  
alkoxy or (C<sub>1</sub>-C<sub>7</sub>)-alkoxycarbonyl,
- (C<sub>1</sub>-C<sub>10</sub>)-alkoxycarbonyl,
- substituted (C<sub>1</sub>-C<sub>10</sub>)-alkoxycarbonyl
- (C<sub>6</sub>-C<sub>14</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl, (C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl-(C<sub>1</sub>-C<sub>8</sub>)-alkyl or (C<sub>1</sub>-C<sub>10</sub>)  
substituted by possibly protected amino and hydroxy,
- 9-flourenylmethoxycarbonyl,
- ketohexosyl,
- ketopentosyl,
- deoxyhexoketosyl,
- dexoypentoketosyl,
- aldohexosyl,
- aldopentosyl,
- deoxyhexoaldosyl,
- deoxypentoaldosyl,
- 2-amino-2-deoxyhexosyl

- 2-acetamido-2-dexoyhexosyl,
- lactosyl or
- maltosyl, it being possible for the joined sugar to be present in the pyranose or furanose form,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- het-carbonyl or -sulfonyl,
- het-(C<sub>1</sub>-C<sub>6</sub>)-alkylcarbonyl or -sulfonyl,
- het-mercapto-(C<sub>1</sub>-C<sub>6</sub>)-alkylcarbonyl or -sulfonyl,

het in each case standing for

furyl, thienyl, benzothienyl, benzodioxolanyl, pyrrolyl, imidazolyl, isoxazolyl, thiazolyl, pyrazolyl, triazolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazinyl, pyrrolidyl, piperidyl, piperazinyl, morpholino, thiomorpholino, tetrahydrofuryl, tetrahydropyryl, tetrahydrothienyl, indolyl, quinolyl or isoquinolyl,

it also being possible for these to be substituted by one or two identical or different radicals from the group (C<sub>1</sub>-C<sub>4</sub>)-alkyl,

(C<sub>1</sub>-C<sub>4</sub>)-alkoxy, (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino, hydroxy, amino, mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino and oxido;

R<sup>2</sup> and R<sup>2\*</sup>

independent of each other mean

- hydrogen,
- carboxyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkyl, which is possibly substituted by up to 2 identical or different radicals from the series
- hydroxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,

- (C<sub>1</sub>-C<sub>4</sub>)-alkylthio,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfinyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy,
- carboxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl,
- amino,
- amidino,
- guanidino,
- N,N'-di-(benzyloxycarbonyl)-guanidino,
- carbamoyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkoxycarbonyl,
- (C<sub>1</sub>-C<sub>5</sub>)-alkoxycarbonylamino,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkoxycarbonylamino, or
- (C<sub>3</sub>-C<sub>10</sub>)-cycloalkyl,
- (C<sub>3</sub>-C<sub>10</sub>)-cylcoalkyl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-(C<sub>3</sub>-C<sub>10</sub>)-cylcoalkyl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl,
- (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>3</sub>)-alkyl, the aryl part possibly being substituted by one, two or three identical or different radicals from the series
- F, Cl, Br,
- hydroxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxy,
- (C<sub>1</sub>-C<sub>4</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl and
- amino, or

- het-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, het being defined as for R<sup>1</sup> or R<sup>1\*</sup>,  
R<sup>3</sup> and R<sup>3\*</sup>

independent of each other mean

- hydrogen or

- methyl,

R<sup>4</sup> and R<sup>4\*</sup>

independent of each other mean

- hydrogen or

- methyl,

R<sup>5</sup>, R<sup>5\*</sup> and R<sup>5\*\*</sup>

independent of one another mean

- hydrogen,

- hydroxy,

- amino or

- carboxy;

R<sup>6</sup>, R<sup>6\*</sup> and R<sup>6\*\*</sup>

independent of one another mean

- hydrogen or

- methyl;

R<sup>7</sup> means

- hydrogen,

- hydroxy or

- methyl;

R<sup>8</sup> and R<sup>8\*</sup>

independent of each other mean

- hydrogen,

- methyl, ethyl or n-propyl, or together with R<sup>9</sup> or R<sup>9\*</sup> and the atoms carrying these form a 1,2,3,4-tetrahydroisoquinoline or a 2-azabicyclooctane skeleton;  
R<sup>9</sup> and R<sup>9\*</sup>

independent of each other are defined like R<sup>2</sup> and R<sup>2\*</sup> in claim 4, or mean  
(C<sub>1</sub>-C<sub>8</sub>)-alkanoyloxy or

together with R<sup>10</sup> or R<sup>10\*</sup> and the atoms carrying these form cyclic ring systems with 5 to 7 ring members;

or together with R<sup>11</sup> or R<sup>11\*</sup> form a thiochroman system the sulfur atom of which can if appropriate be oxidized to sulfone;

R<sup>10</sup> and R<sup>10\*</sup>

independent of each other mean

- hydrogen or

- methyl;

R<sup>11</sup> and R<sup>11\*</sup> are defined as in claim 4;

in the aforementioned compounds of formula I one or more amide groups (-CONH-) of the main chain can be replaced as defined in claim 4;

R<sup>14</sup> stands for

- hydrogen or

- methyl;

as well as their physiologically tolerated salts.

6. Process for the production of a compound of formula I as contained in claims 1 to 5, characterized in that

R<sup>1</sup> and R<sup>1\*</sup>

independent of each other stand for

a<sub>1</sub>) - hydrogen,

- carboxyl,

- 207



- piperidyl,
- morpholino,
- quinolyl or
- isoquinolyl,

and also possibly being substituted by one or two identical or different radicals from the group (C<sub>1</sub>-C<sub>4</sub>)-alkyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino, hydroxy, amino, mono- or di-(C<sub>1</sub>-C<sub>4</sub>)-alkylamino;

 $R^2$  and  $R^{2*}$ 

independent of each other stand for

- hydrogen,
- carboxyl,
- methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec.-butyl, n-pentyl, n-hexyl,
- cyclohexyl,
- cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl,
- 4-methylcyclohexylmethyl,
- 1-decahydronaphthylmethyl, 2-decahydronaphthylmethyl,
- phenyl,
- benzyl,
- 2-phenylethyl,
- 1-naphthylmethyl, 2-naphthylmethyl,
- 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl,
- 2,4,6-trimethylbenzyl,
- 4-tert.-butylbenzyl,
- 4-tert.-butoxybenzyl
- 4-hydroxybenzyl,

- 4-methoxybenzyl,
- 2,4-dimethoxybenzyl,
- 3,4-dihydroxybenzyl,
- 3,4-dimethoxybenzyl,
- (benzodioxolane-5-yl)methyl,
- 4-chlorobenzyl,
- hydroxymethyl,
- 1-hydroxyethyl,
- 4-pyridyl,
- 4-(N-oxidopyridyl),
- 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, 2-(4-pyridyl)-ethyl,
- 2-thienylmethyl, 3-thienylmethyl,
- 2-(2-thienyl)ethyl, 2-(3-thienyl)ethyl,
- indole-2-yl-methyl, indole-3-yl-methyl,
- (1-methyl-imidazole-4-yl)methyl,
- imidazole-4-yl-methyl, imidazole-1-yl-methyl,
- 2-thiazolylmethyl,
- 3-pyrazolylmethyl,
- 4-pyrimidylmethyl,
- 2-benzo[b]thienylmethyl, 3-benzo[b]thienylmethyl,
- 2-furylmethyl,
- 2-(methylthio)ethyl,
- 2-(methylsulfinyl)ethyl,
- 2-(methylsulfonyl)ethyl,

R<sup>3</sup>, R<sup>3\*</sup>, R<sup>4</sup>, R<sup>4\*</sup>, R<sup>6</sup>, R<sup>6\*</sup>, R<sup>10</sup> and R<sup>10\*</sup>

mean hydrogen;

$R^5$  and  $R^{5*}$

independent of each other stand for

- hydrogen,
- hydroxy or
- amino;

$R^7$  means

- hydroxy or
- methyl;

$R^8$  and  $R^{8*}$

independent of each other mean

- hydrogen or

together with  $R^9$  or  $R^{9*}$  and the atoms carrying these form a 1,2,3,4-tetrahydroisoquinoline or 2-azabicyclooctane skeleton;

$R^9$  and  $R^{9*}$

independent of each other are defined like  $R^2$  or  $R^{2*}$  or mean

- hydroxy,
- acetoxy,
- tert.-butoxymethyl,
- 3-guanidinopropyl,
- carbamoylmethyl, carbamoylethyl,
- carboxymethyl, carboxyethyl,
- mercaptomethyl,
- (1-mercapto-1-methyl)ethyl,
- aminomethyl, 2-aminoethyl, 3-aminopropyl, 4-aminobutyl,
- N,N-dimethylamino,

- N,N'-di-(benzyloxycarbonyl)-guanidino-propyl,
- 2-benzyloxycarbonylethyl, benzyloxycarbonylmethyl,
- tert.-butylsulfonylmethyl

or

- 4-benzylcarbonylaminobutyl;

R<sup>11</sup> and R<sup>11\*</sup>

independent of each other mean

- hydrogen,
- hydroxy or
- acetoxy,

and in the aforementioned compounds of this invention one or more amide groups (-CONH-) of the main chain can be replaced by -CH<sub>2</sub>NR<sup>14</sup>- or -CH(OH)CH<sub>2</sub>-;

R<sup>14</sup> stands for

- hydrogen or
- methyl;

as well as their physiologically tolerated salts.

7. Process for the production of a compound of formula I as contained in claims 1 to 6, characterized in that

R<sup>1</sup> and R<sup>1\*</sup>

independent of each other stand for

- a<sub>1</sub>) - hydrogen,
- carboxyl,
- (C<sub>1</sub>-C<sub>16</sub>)-alkylsulfonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-mono- or -dihydroxyalkylsulfonyl,
- mono-, di- or trihydroxy-(C<sub>1</sub>-C<sub>3</sub>)-alkyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkoxycarbonyl,

- (C<sub>1</sub>-C<sub>14</sub>)-alkanoyl,
  - amino-(C<sub>1</sub>-C<sub>12</sub>)-alkanoyl,
  - (C<sub>6</sub>-C<sub>10</sub>)-aryl-(C<sub>1</sub>-C<sub>4</sub>)-alkylcarbonyl,
  - 9-fluorenylmethoxycarbonyl,
  - (C<sub>1</sub>-C<sub>4</sub>)-alkanoyloxy-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
  - 1,2-diacetoxyethyl,
  - 1,2,3-triacetoxypropyl,
  - phenyl
  - benzolsulfonyl possibly substituted by halogen, amino, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or methoxy,
  - benzolsulfonyl, -sulfinyl or -thio possibly substituted by halogen, amino, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or methoxy,
  - het or het-sulfonyl,
  - het-(C<sub>1</sub>-C<sub>4</sub>)-alkanoyl,
  - het-mercapto-(C<sub>1</sub>-C<sub>3</sub>)-alkylcarbonyl,
- het in each case standing for
- pyrrolyl,
  - imidazolyl,
  - pyridyl,
  - pyrimidyl,
  - pyrrolidyl,
  - quinolyl,
  - isoquinolyl,
  - piperidyl or
  - morpholino,

it also being possible that this radical is substituted by one or two identical or different radicals from the group methyl, amino and (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,

- amino-(C<sub>3</sub>-C<sub>6</sub>)-cycloalkylcarbonyl,
- (C<sub>1</sub>-C<sub>8</sub>)-alkanoyl, which is substituted by hydroxy and amino and possibly by phenyl or cyclohexyl,
- possibly protected amino-substituted phenyl- or cyclohexyl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl,
- amino,
- (C<sub>1</sub>-C<sub>4</sub>)-alkoxycarbonylamino,
- benzyloxycarbonylamino,
- 1-deoxyhexoketosyl or 1-deoxypentoketosyl,
- hexosyl or pentosyl,

it being possible for the joined sugars to be present in the pyranose or the furanose form,

R<sup>2</sup> and R<sup>2\*</sup>

independent of each other stand for

- hydrogen,
- methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec.-butyl, pentyl, hexyl,
- cyclopentylmethyl, cyclohexylmethyl,
- 4-methylcyclohexylmethyl,
- benzyl,
- 2-phenylethyl,
- 1-naphthylmethyl, 2-naphthylmethyl,
- 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl,

- 2,4,6-trimethylbenzyl,
- 4-tert.-butylbenzyl,
- 4-methoxybenzyl,
- 3,4-dihydroxybenzyl,
- 2,4-dimethoxybenzyl,
- 3,4-dimethoxybenzyl,
- 3,4-dimethylenedioxybenzyl,
- 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl or
- 2-(4-pyridyl)ethyl;

$R^3$ ,  $R^{3*}$ ,  $R^4$ ,  $R^{4*}$ ,  $R^6$ ,  $R^{6*}$ ,  $R^7$ ,  $R^{10}$  AND  $R^{10*}$

mean hydrogen;

$R^5$  and  $R^{5*}$

independent of each other mean

- hydrogen or
- hydroxy;

$R^8$  and  $R^{8*}$  independent of each other are defined as in claim 6,

$R^9$  and  $R^{9*}$

independent of each other are defined like  $R^9$  and  $R^{9*}$  in claim 6;

$R^{11}$  and  $R^{11*}$  independent of each other are defined as in claim 6,

as well as their physiologically tolerated salts.

8. Process for the production of a compound of formula I as contained in claims 1 to 7, characterized in that

Y stands for a radical of formula III;

l means 0 or 1;

m means 1;

A,  $A^*$ , D and  $D^*$  are defined as in claim 1;

n, n\*, o, o\*, p and p\* independent of one another mean 1;

E, E\*, F, F\*, G and G\* independent of one another stand for an amino acid from the series Val, Lys, Lys(Z), Phe, Chg, Ser, Asn, Gly, Ile, Tbg, Nva or Npg;

R<sup>1</sup> and R<sup>1\*</sup> independent of each other mean

- hydrogen,
- carboxyl,
- methylsulfonyl,
- tert.-butylsulfonyl,
- tert.-butoxycarbonyl,
- 2-hydroxyethylsulfonyl,
- 1,2,3-trihydroxypropyl,
- 1,2,3-triacetoxypropyl,
- benzyloxycarbonyl,
- 4-methylphenylsulfonyl,
- 4-chlorobenzylthio,
- benzylsulfinyl,
- 4-chlorobenzylsulfonyl,
- hexadecylsulfonyl,
- 4-amino-1-piperidyl-sulfonyl,
- N-tert.-butoxycarbonyl-4-amino-1-piperidyl-sulfonyl,
- 4-amino-1-piperidyl-carbonyl,
- N-tert.-butoxycarbonyl-4-amino-1-piperidyl-carbonyl,
- 2-amino-3-phenyl-propyl,
- N-tert.-butoxycarbonyl-2-amino-3-phenyl-propyl,
- 2-amino-1-hydroxy-4-methyl-pentyl,
- deoxyfructos-1-yl,

- mannofuranosyl,
- 4-aminocyclohexylcarbonyl,
- 2-pyridylacetyl,
- 4-pyridylthio-acetyl,
- 2-quinolylcarbonyl,
- 1-naphthylacetyl,
- 1-naphthyloxyacetyl,
- 1-(4-pyridyl)-ethylsulfonyl,
- 12-aminododecanoyl,
- 4-(N-oxidopyridyl),
- 4-pyridyl,
- tetradecanoyl,
- phenyl,
- amino or

- tert.-butoxycarbonylamino;

$R^2$  and  $R^{2*}$  independent of each other mean

- hydrogen,
- 2-(4-pyridyl)ethyl,
- isopropyl,
- isobutyl,
- n-pentyl,
- benzyl,
- 3,4-methylenedioxybenzyl,
- 2,4-dimethoxybenzyl,
- 4-tert.-butylbenzyl,
- 2-phenylethyl or

- cyclohexylmethyl;

$R^3$ ,  $R^{3*}$ ,  $R^4$ ,  $R^{4*}$ ,  $R^6$ ,  $R^{6*}$ ,  $R^7$ ,  $R^{10}$  and  $R^{10*}$  mean

- hydrogen;

$R^5$  and  $R^{5*}$  independent of each other mean

- hydrogen or

- hydroxy;

$R^8$  and  $R^{8*}$  mean

- hydrogen, or together with  $R^9$  or  $R^{9*}$  and the atoms carrying these form a 1,2,3,4-tetrahydroquinoline-3,4-diyl system;

$R^9$  and  $R^{9*}$  independent of each other mean

- hydrogen,

- hydroxy,

- acetoxy,

- n-propyl,

- isopropyl,

- isobutyl,

- aminomethyl,

- 4-aminobutyl,

- hydroxymethyl,

- tert.-butoxymethyl,

- aminocarbonylmethyl,

- 2-benzoyloxycarbonyl-ethyl,

- 4-benzoylcarbonylamino-butyl,

- N,N'-di(benzoyloxycarbonyl)-guanidino-propyl,

- cyclohexyl,

- cyclohexylmethyl,

- benzyl,
- 2-phenyl-ethyl,
- 4-hydroxy-benzyl,
- 4-methoxy-benzyl,
- 4-tert.-butoxy-benzyl,
- 1-naphthylmethyl,
- 2-thienylmethyl,
- 1-imidazolyl-methyl,
- 3-indolyl-methyl,
- 4-pyridylmethyl,
- 4-(N-oxidopyridyl)methyl,
- 2-methylthio-ethyl,
- 2-methylsulfonyl-ethyl,
- tert.-butylsulfonyl-methyl or
- 2-carboxyl-ethyl;

$R^{11}$  and  $R^{11*}$  independent of each other mean

- hydrogen
- hydroxy or
- acetoxy;

it being possible in the aforementioned compounds that one or more amide groups (-CONH-) of the main chain are replaced by -CH<sub>2</sub>NH- or -CH(OH)CH<sub>2</sub>-; as well as their physiologically tolerated salts.

9. Process for the production of a compound of formula I as contained in claims 1 to 8, characterized in that

$l = 0$ ;

$m = 1$ ;

$$n + o + p = 1;$$

D and D\* stand for a radical of formula VI or VI\*;

R<sup>1</sup> and R<sup>1\*</sup> mean

- (C<sub>1</sub>-C<sub>12</sub>)-alkylsulfonyl, which can possibly be substituted by up to 3 identical or different radicals from the series

- hydroxy,

- amino or

- carboxy;

R<sup>2</sup> and R<sup>2\*</sup> independent of each other mean

- hydrogen,

- carboxyl,

- methyl, ethyl, isopropyl, n-propyl, n-butyl, isobutyl, sec.-butyl, pentyl, hexyl,

- cyclohexyl,

- cyclopentylmethyl, cyclohexylmethyl, cycloheptylmethyl,

- 4-methylcyclohexylmethyl,

- 1-decahydronaphthylmethyl, 2-decahydroanaphthylmethyl,

- phenyl,

- benzyl,

- 2-phenylethyl,

- 1-naphthylmethyl, 2-naphthylmethyl,

- 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl,

- 2,4,6-trimethylenzyl,

- 4-tert.-butylbenzyl,

- 4-tert.-butoxybenzyl,

- 4-hydroxybenzyl,

- 4-methoxybenzyl,
- 2,4-dimethoxybenzyl,
- 3,4-dihydroxybenzyl,
- 3,4-dimethoxybenzyl,
- (benzodioxolane-4-yl)methyl,
- 4-chlorobenzyl,
- hydroxymethyl,
- 1-hydroxyethyl,
- 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, 2-(4-pyridyl)-ethyl,
- 2-thienylmethyl, 3-thienylmethyl,
- 2-(2-thienyl)ethyl, 2-(3-thienyl)ethyl,
- indole-2-yl-methyl, indole-3-yl-methyl,
- (1-methyl-imidazole-4-yl)methyl,
- imidazole-4-yl-methyl, imidazol-1-yl-methyl,
- 2-thiazolylmethyl,
- 3-pyrazolylmethyl,
- 4-pyrimidylmethyl,
- 2-benzo[b]thienylmethyl, 3-benzo[b]thienylmethyl,
- 2-furylmethyl,
- 2-(methylthio)ethyl,
- 2-(methylsulfinyl)ethyl or
- 2-(methylsulfonyl)ethyl;

R<sup>3</sup>, R<sup>3\*</sup>, R<sup>4</sup>, R<sup>4\*</sup>, R<sup>6</sup>, R<sup>6\*</sup>, R<sup>11</sup> an R<sup>11\*</sup> mean

- hydrogen;

R<sup>5</sup> and R<sup>5\*</sup> mean

- hydroxy;

R<sup>9</sup> and R<sup>9\*</sup>

are defined as in claim 8;

as well as their physiologically tolerated salts.

10. Process for the production of a pharmaceutical agent containing a compound of formula I as contained in claims 1 to 8, characterized in that it, and possibly one or more carriers, are brought into a form suitable for administering it.

11. Use of a compound of formula I as contained in claims 1 to 9 as a drug.

12. Use of a compound of formula I as contained in claims 1 to 9 for inhibiting retroviral proteases.

13. Use of a compound of formula I as contained in claims 1 to 9 in the treatment of "acquired immune deficiency syndrome."

